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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated

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NEWS 39   May 16  CHEMREACT will be removed from STN
NEWS 40   May 19  Simultaneous left and right truncation added to WSCA
NEWS 41   May 19  RAPRA enhanced with new search field, simultaneous left and
                  right truncation
NEWS 42   Jun 06  Simultaneous left and right truncation added to CBNB
NEWS 43   Jun 06  PASCAL enhanced with additional data
NEWS 44   Jun 20  2003 edition of the FSTA Thesaurus is now available
NEWS 45   Jun 25  HSDB has been reloaded

NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
              MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
              AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS    STN Operating Hours Plus Help Desk Availability
NEWS INTER    General Internet Information
NEWS LOGIN    Welcome Banner and News Items
NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
NEWS WWW      CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 17:40:02 ON 26 JUN 2003

=> file .biotech caplus
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILES 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 17:40:16 ON 26 JUN 2003
ALL COPYRIGHTS AND RESTRICTIONS APPLY.  SEE HELP USAGETERMS FOR DETAILS.

7 FILES IN THE FILE LIST

=> christians F?/au or cole K?/au
CHRISTIANS IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s christians F?/au or cole K?/au
L1        2293 CHRISTIANS F?/AU OR COLE K?/AU

=> s oligo tag# or nucleic acid tag# or oligonucleotide tag#
L2         197 OLIGO TAG# OR NUCLEIC ACID TAG# OR OLIGONUCLEOTIDE TAG#

=> s l1 and (screen### (4a) polpeptide#)
L3           0 L1 AND (SCREEN### (4A) POLPEPTIDE#)

=> s l1 and l2
L4           1 L1 AND L2
```

=> d all

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN 2003:355701 CAPLUS
DN 138:365121
TI Methods for screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays
IN **Christians, Fred; Cole, Kyle B.**
PA USA
SO U.S. Pat. Appl. Publ., 24 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM C12Q001-68
ICS A61K038-14; C07K009-00
NCL 435006000; 530322000; 530395000
CC 9-2 (Biochemical Methods)
Section cross-reference(s): 3
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003087232	A1	20030508	US 2002-683613	20020124
PRAI US 2001-264635P	P	20010125		

AB In one aspect of the invention, methods are provided for the creation and screening of polypeptides that eliminates bacterial cloning and individual screening. In preferred embodiments, the method involves partnering each protein with a unique DNA **oligonucleotide tag** that directs the protein to a unique site on the microarray due to specific hybridization with a complementary tag-probe on the array.
ST screening polypeptide **oligonucleotide tag** immobilization probe microarray
IT Affinity
(binding; screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)
IT High throughput screening
(drug; screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)
IT mRNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(encoding polypeptide and labeled with **oligonucleotide tag**; screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)
IT Gene
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(expression; screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)
IT Drug screening
(high throughput; screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)
IT Drugs
(immobilized polypeptide binding affinity for; screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)
IT Ligands
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(immobilized polypeptide binding affinity for; screening polypeptides using **oligonucleotide tags** and immobilization on

probe arrays)

IT DNA
RL: ARG (Analytical reagent use); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); USES (Uses)
(immobilized; screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)

IT Peptides, analysis
Proteins
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(labeled, with **oligonucleotide tags**; screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)

IT Translation, genetic
(of oligonucleotide-tagged mRNA encoding polypeptide; screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)

IT DNA microarray technology
Gene expression profiles, animal
High throughput screening
Human
Immobilization, molecular
Nucleic acid hybridization
PCR (polymerase chain reaction)
(screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)

IT Peptides, analysis
Proteins
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation)
(screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); USES (Uses)
(screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)

IT Oligonucleotides
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(tags; screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)

IT 521340-66-9 521340-67-0 521340-68-1 521340-69-2 521340-70-5
521340-71-6 521340-72-7 521340-73-8 521340-74-9 521340-75-0
521340-76-1 521340-77-2 521340-78-3 521340-79-4 521340-80-7
521340-81-8 521340-82-9 521340-83-0
RL: PRP (Properties)
(unclaimed nucleotide sequence; methods for screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)

IT 521339-41-3
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(unclaimed nucleotide sequence; screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays)

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=> d his

     (FILE 'HOME' ENTERED AT 17:40:02 ON 26 JUN 2003)

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 17:40:16 ON 26 JUN 2003
L1          2293 S CHRISTIANS F?/AU OR COLE K?/AU
L2           197 S OLIGO TAG# OR NUCLEIC ACID TAG# OR OLIGONUCLEOTIDE TAG#
L3             0 S L1 AND (SCREEN### (4A) POLPEPTIDE#)
L4             1 S L1 AND L2

=> s (screen### (4a) polpeptide#)
L5             0 (SCREEN### (4A) POLPEPTIDE#)

=> s (screen### (4a) polypeptide#)
L6          1884 (SCREEN### (4A) POLYPEPTIDE#)

=> s l6 and l2
L7             2 L6 AND L2

=> d ibib abs l7 1-2

L7   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2003:355701  CAPLUS
DOCUMENT NUMBER:          138:365121
TITLE:                    Methods for screening polypeptides
                          using oligonucleotide tags and
                          immobilization on probe arrays
INVENTOR(S):              Christians, Fred; Cole, Kyle B.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 24 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     US 2003087232      A1   20030508      US 2002-683613   20020124
PRIORITY APPLN. INFO.:                   US 2001-264635P  P  20010125
AB   In one aspect of the invention, methods are provided for the creation and
     screening of polypeptides that eliminates bacterial
     cloning and individual screening.  In preferred embodiments, the method
     involves partnering each protein with a unique DNA oligonucleotide
     tag that directs the protein to a unique site on the microarray
     due to specific hybridization with a complementary tag-probe on the
array.

L7   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2001:247548  CAPLUS
DOCUMENT NUMBER:          134:276473
TITLE:                    Compounds displayed on replicable genetic packages
                          (such as bacteriophage) and methods of using same for
                          drug discovery
INVENTOR(S):              Barrett, Ronald W.; Dower, William J.; Gallop, Mark;
                          Woiwode, Thomas F.; Cwirla, Steven E.
PATENT ASSIGNEE(S):       Xenoport, Inc., USA
```

SOURCE: PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001023619	A1	20010405	WO 2000-US26849	20000929
WO 2001023619	C2	20021212		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1224327	A1	20020724	EP 2000-968494	20000929

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: US 1999-156675P P 19990929
WO 2000-US26849 W 20000929

AB Replicable genetic packages and collections thereof that display various compds. are provided. Examples of replicable genetic packages include viruses, bacteriophage, bacteria, spores and cells. In case of bacteriophage, replicable genetic package can be either a filamentous phage (e.g. fd, f1, Md13) or a non-filamentous phage such as T7 or lambda.

In some instances, the replicable genetic packages include **nucleic acid tags** that serve to record a characteristic of the compd. or compds. that are attached to the replicable genetic package. The invention further provides a no. of different methods for using the replicable genetic packages to screen a library of compds. for a desired biol. activity. The methods of the invention are typically used for **screening** compds. other than expressed **polypeptides** because expressed **polypeptides** can be **screened** by conventional phage display methods.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 17:40:02 ON 26 JUN 2003)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS' ENTERED AT 17:40:16 ON 26 JUN 2003

L1 2293 S CHRISTIANS F?/AU OR COLE K?/AU
L2 197 S OLIGO TAG# OR NUCLEIC ACID TAG# OR OLIGONUCLEOTIDE TAG#
L3 0 S L1 AND (SCREEN### (4A) POLPEPTIDE#)
L4 1 S L1 AND L2
L5 0 S (SCREEN### (4A) POLPEPTIDE#)
L6 1884 S (SCREEN### (4A) POLYPEPTIDE#)
L7 2 S L6 AND L2

=> s probe array or array or microarray or GeneChip or GenFlex array or chip

```
L8      319682 PROBE ARRAY OR ARRAY OR MICROARRAY OR GENECHIP OR GENFLEX
ARRAY
               OR CHIP

=> s ((plurality or multiple or mixture) (4a) polypeptide#)
L9        2795 ((PLURALITY OR MULTIPLE OR MIXTURE) (4A) POLYPEPTIDE#)

=> s l9 and l8
L10         56 L9 AND L8

=> l10 and l2
L10 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l10 and l2
L11          0 L10 AND L2

=> s l10 and tag
L12          6 L10 AND TAG

=> d ibib abs l12 1-6

L12   ANSWER 1 OF 6  BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2003-14319  BIOTECHDS
TITLE:            Printed material useful as a delivery and storage system for
                  oligomer and/or polymer, comprises a support having an
                  oligomer and/or polymer applied on it;
                     printed material, and DNA amplification for use in
                     diagnosis
AUTHOR:           HAYASHIZAKI Y
PATENT ASSIGNEE:  DNAFORM KK; RIKEN KK
PATENT INFO:      WO 20030027991 3 Apr 2003
APPLICATION INFO: WO 2002-JP9766 24 Sep 2002
PRIORITY INFO:    JP 2001-291249 25 Sep 2001; JP 2001-291249 25 Sep 2001
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2003-354676 [33]
AN    2003-14319  BIOTECHDS
AB    DERWENT ABSTRACT:
      NOVELTY - A printed material (1) (I) comprising at least one support
      having at least one oligomer and/or polymer applied on it, is new.
           DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1)
      preparing (I) involves applying the oligomer and/or polymer on the
      support before or after printing; (2) delivering (M1) and/or storing at
      least one oligomer and/or polymer applied on at least one support for a
      printed material, comprising applying the oligomer and/or polymer on the
      support before or after printing and delivering or storing the printed
      material; (3) synthesis (M2) of cDNA, comprising: (a) applying at least
a
      set of primers for the amplification and/or ligation of exons of a
      support and/or printed material; (b) recovering the at least set of
      primers from the support and/or printed material; (c) mixing the set of
      primers with template DNA, enzyme and buffer; and (d) carrying out the
      amplification and/or ligation; (4) a kit comprising a support and/or
      printed material comprising at least one primer or a set of primers
      applied on it; and (5) a kit for the synthesis of cDNA and/or
full-length
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cDNA from genomic template, comprising at least one support and/or printed material comprising at least one set of primers, for the amplification and/or ligation of exons, applied on it.

BIOTECHNOLOGY - Preferred Material: The printed material is in unbound form, or in bound form where the support is not bound in the material or the support is bound as a page of the bound material. Optionally, (I) comprises at least two supports which are not bound together. The printed material is composed of at least one printed page. The printed material is chosen from journals, magazines, articles, books, booklets, leaflets, pamphlets, reports, posters, cards and labels. The support is a water-insoluble, water-dissolvable and/or water-soluble support. The water-insoluble support comprises cellulose as a major component. The water-soluble support is in the form of wafer. Preferably, the support is in the form of card(s). The oligomer is chosen from oligonucleotide, oligopeptide, oligosaccharide, peptide nucleic acid (PNA) or its mixture. The polymer is chosen from polynucleotide, **polypeptide**, polysaccharide, PNA or its **mixture**. The oligomer or polymer is a fragment or a complete molecule. The oligonucleotide or polynucleotide is selected from genomic DNA, cDNA, RNA, mRNA, PNA or its combination. Preferably, the oligonucleotide or polynucleotide is chosen from a fragment, an expressed sequence **tag** (EST) sequence, long strand, full-coding and full-length sequence. The oligonucleotide or polynucleotide comprises one or more amplification and/or ligation primer and/or oligonucleotide probe(s). (I) comprises a set of primers for the amplification and ligation of exons of a gene comprised in genomic DNA. The set of primers comprises a pair of primers for each exon of the desired gene, at least one primer of each pair of one exon being also partially complementary to the next exon. The set of primers are suitable for synthesizing cDNA and/or full-length cDNA from genomic DNA by amplification and ligation of the exons of a gene. (I) further comprises one or more enzymes and/or buffer. Preferred Method: The oligomer and/or polymer is applied on the support by fixing or printing it on the support. In (M1), the oligomer and/or polymer is applied on the support by applying or adhering a solution of the oligomer and/or polymer directly to the support by a pin, syringe or ink-jet printer. (M1) further involves recovering the oligomer and/or polymer by elution from the support. The recovery is carried out by inserting the support in a device and performing the elution and recovery from the support automatically by the device. The support is preferably in the form of card which comprises a bar- code, a **chip** or a label containing information about the position of the oligomer and/or polymer on the card. The operator selects the oligomer and/or polymer of interest and the device automatically elutes and recovers the oligomer and/or polymer of interest from the support. In (M2), after the application step, the support and/or printed material is stored and/or delivered. The enzyme and buffer are applied on the support and/or printed material during application step. Preferred Kit: The support and/or material further comprises at least one of enzyme, buffer, genomic DNA, cDNA, RNA, mRNA, PNA, plasmid, vector and nucleic acid. The kit for synthesis of cDNA further comprises at least one enzyme for the amplification and/or

ligation step, and/or buffer.

USE - (M2) is useful for synthesizing DNA, where the product of amplification and/or ligation is cDNA and/or full- length cDNA which is recovered and used for determination of nucleotide insertion/deletion, single nucleotide polymorphism (SNP) and sequencing analysis, in a diagnostic method for determination of nucleotide insertion/deletion, or SNP analysis. Optionally, the cDNA and/or full-length cDNA is useful for the peptide, polypeptide or protein expression. (All claimed.) The printed material is useful in research applications, or for providing scientists with oligomer and/or polymers from the printed materials easily and immediately.

ADVANTAGE - From the printed material, at least an oligomer and/or polymer can be obtained immediately and directly, without need to make a request for it. The oligomers and/or polymers can be delivered and stored easily with reduced labor and time while eliminating the need to use special equipment or facilities. Thus, the printed material is a quick, efficient and inexpensive sample delivery system.

EXAMPLE - Three RIKEN plasmid cDNA clones with various cDNA insert sizes (744, 2440 and 5460 base pairs) were inserted into pBluescript. Plasmid DNA comprising the cDNA clones were purified. The plasmid DNA was dissolved in TE (10 mM Tris-HCl (pH 8.0), 1 mM EDTA). DNA concentration was adjusted to 0.1 micro-g/micro-l. At this step an inert dye, was added to the solution in order to facilitate identification of spot position on the support at the time of recovery. 0.1 micro-l of the plasmid DNA solution prepared as above was transferred onto 60 MDP paper used as DNA sheet using a 96-pin tool. Spotted positions were easily identified by being spotted in a marked position on the paper. After drying the paper in air for more than 30 minutes, DNA was extracted from the sheet as follows. The piece of 60 MDP paper (0.4x0.4 mm) containing the selected DNA spot was cut out from the sheet and placed into a PCR tube followed by addition of 50 micro-l of PCR solution. PCR solution contained the following PCR primers: 21M13 5'-TGTAAAACGACGGCCAGT-3' and 1233-Rv 5'-AGCGGATAACAATTTCACACAGGA-3', 0.2 mM each of dATP, dGTP, dCTP and dTTP and in presence of various concentrations of MgCl. After centrifuging the resulting solution, the PCR cycle was initiated. Aliquots of PCR solutions were analyzed using 1 % agarose gel electrophoresis. Results showed that the cDNA inserts were amplified successfully, preferably at Mg2+ concentration of 5.3 mM. This test confirmed that the chosen conditions allowed for an efficient spotting and extraction of DNA. (91 pages)

L12 ANSWER 2 OF 6 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2003-06325 BIOTECHDS
TITLE: Protein **array** used to generate a library of target organism polypeptides;
protein **array** and polymerase chain reaction for protein library construction and vaccine design
AUTHOR: FELGNER P L; DOOLAN D L
PATENT ASSIGNEE: GENE THERAPY SYSTEMS INC
PATENT INFO: WO 2002097051 5 Dec 2002
APPLICATION INFO: WO 2002-US17005 29 May 2002
PRIORITY INFO: US 2001-294739 30 May 2001; US 2001-294739 30 May 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-041408 [03]

AN 2003-06325 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - A method for generating a library of target organism polypeptides, is new.

DETAILED DESCRIPTION - A method for generating (I) a library of target organism polypeptides comprising: (a) performing a first PCR reaction using a first primer pair capable of amplifying a desired polynucleotide sequence form the target organism to provide an amplified coding sequence which amplified coding sequence is not transcriptionally active; (b) providing a second PCR nucleotide primer pair capable of adding at least on e nucleotide sequence that confers transcriptional activity to the amplified coding sequence; (c) performing a second PCR with the second primer pair and the amplified coding sequence thereby resulting in amplification of a transcriptionally active coding sequence;

(d) expressing the polypeptide of the transcriptionally active coding sequence; and (e) repeating steps (a)-(d) at least 10 times with different first primer pairs to express different polypeptides of said target organism.INDEPENDENT CLAIMS are also included for the following: (1) screening (II) a library or target organism polypeptides in order to identify a target organism antigen that is capable of eliciting a humoral

immune response: (a) providing a library of target organism polypeptides attached to a linker molecule prepared by (I); (b) immobilizing at least 10 of the target organism polypeptides to a solid support; and (c) assaying the polypeptides with at least one antibody from an animal that has been immunized with one or more antigens from the target organism to identify a target organism antigen capable of eliciting a humoral immune response. (2) screening (III) a library or target organism polypeptides in order to identify a target organism antigen that is capable of eliciting a cell-mediated immune response: (a) providing a library of target organism polypeptides attached to a linker molecule prepared by (I); (b) delivering at least 10 of the target organism **polypeptides** into a **plurality** of antigen-presenting cells; and (c) assaying the antigen-presenting cells with at least one T- cell from an animal that has been immunized with one or more antigens from the target organism to identify a target organism antigen capable of

eliciting a cell-mediated immune response. (3) developing a subunit vaccine against a target organism; (4) an **array** of at least 20 target organism polypeptides prepared by (I); (5) screening an **array** in order to identify a target organism antigen; and (6) an automated system capable of performing (I).

BIOTECHNOLOGY - Preferred Method: (I) Steps are repeated at least 266 times. The target organism is vaccinia virus, B. antracis, Francisella tularensis, P. falciparum or Mycobactreium tuberculosis.Further comprises adding at least one polynucleotide operably encoding a linker molecule producing a target organism polypeptide attached to a linker molecule. The linker molecule is an epitope or is selected from 6x, 7x, 8x, 9x and 10x his-**tag**, GST **tag**, fluorescent protein **tag**, Flag **tag** and HA **tag**. At least one sequence that confers transcriptional activity is a promoter or terminator sequence. Designing the first primer pair and

the PCR (polymerase chain reaction) is performed using an automated system. (II) and (III) antigen-presenting cells are B cells, macrophages or dendritic cells. The target organism is vaccinia virus. Preferred **Array**: the **array** comprises a plurality of sub arrays and are microtitre plates of 96 wells.

USE - Generating a library of target organism polypeptides and

screening (III) a library or target organism polypeptides in order to identify a target organism (claimed).

EXAMPLE - No suitable example is given in the specification.(60 pages)

L12 ANSWER 3 OF 6 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2003-01246 BIOTECHDS
TITLE: Host cell useful for monitoring the solubility of a target protein and in identifying mutations in the cell, comprises a solubility reporter nucleic acid and a target polypeptide-expressing nucleic acid; vector expression in host cell, DNA library screening for mutation detection and antibiotic agent identification
AUTHOR: LESLEY S; KNUTH M
PATENT ASSIGNEE: IRM LLC
PATENT INFO: WO 2002061041 8 Aug 2002
APPLICATION INFO: WO 2001-US51426 21 Nov 2001
PRIORITY INFO: US 2001-324833 24 Sep 2001; US 2000-721340 21 Nov 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-608512 [65]
AN 2003-01246 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A host cell (I) comprising a solubility reporter nucleic acid with a protein solubility responsive promoter that is operably linked to a reporter gene, and a target polypeptide-expressing nucleic acid that comprises a polynucleotide which encodes a target polypeptide, where an expression of the target polypeptide in an insoluble form causes a change in the expression of the reporter gene, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an **array** of two or more populations of (I), where the host cell of each population differs in the target polypeptides expressed by the host cells; (2) determining the solubility of a target polypeptide, comprising: (a) culturing (I) under conditions in which the target polypeptide is expressed; and (b) determining whether the expression of the reporter gene is increased or decreased, thus, determining the solubility of the expressed target polypeptide; (3) identifying mutations in a cell that alter the solubility of a target polypeptide, comprising: (a) treating a cell with a mutagen; (b) introducing the above solubility reporter nucleic acid and target polypeptide-expressing nucleic acid into the cell; (c) culturing the cell under conditions favorable for expression of the target polypeptide; (d) measuring the expression of the reporter gene; and (e) comparing the level of expression of the reporter gene in the cell with the level observed in an unmutated cell comprising the above nucleic acids to identify a cell that comprises a mutation that alters the solubility of the target polypeptide; (4) identifying alterations to a polynucleotide that encodes a target polypeptide, and which alters the solubility of the target polypeptide, comprising: (a) altering a polynucleotide that encodes the target polypeptide to form an altered polynucleotide; (b) steps (b)-(d) of method (3); and (c) comparing the level of expression of the reporter gene with the level observed in a cell with an unaltered polynucleotide that encodes the target polypeptide, to identify an alteration to the polynucleotide that changes the solubility of the

encoded target polypeptide; (5) identifying variations in a process for biosynthesis of a target polypeptide that alters the solubility of the target polypeptide, comprising: (a) culturing (I) under alternative conditions in which the target polypeptide is expressed; and (b) comparing the expression of the reporter gene by host cells grown under each of the alternative conditions; (6) screening an expression library to identify library members that express soluble target **polypeptide**, comprising: (a) introducing a **plurality** of expression vectors that comprise a polynucleotide encoding a target **polypeptide** into a **plurality** of (I) to create an expression library; (b) step (a) of method (2); and (c) detecting the expression of the reporter gene, thus, identifying library members that express soluble target polypeptides; (7) identifying an antibiotic agent, comprising: (a) contacting a cell having a solubility reporter nucleic acid with a candidate antibiotic agent, where the nucleic acid comprises a protein solubility responsive promoter operably linked to a reporter gene; and (b) detecting the level of expression of the reporter gene, where a change indicates an agent that inhibits protein folding in the cell; (8) identifying a promoter that is differentially regulated in response to expression of an insoluble polypeptide in a host cell that comprises the promoter, comprising: (a) providing (I); (b) step (a) of method (2); and (c) step (b) of method (2), thus, determining whether the putative protein solubility responsive promoter is differentially regulated in response to expression of an insoluble polypeptide in (I).

BIOTECHNOLOGY - Preferred Host Cell: The host cell comprises a solubility responsive promoter which has a polynucleotide sequence that is at least 75% identical to 9 fully defined sequences comprising 200 bp given in the specification, or to 13 fully defined sequences comprising 300 bp given in the specification. The solubility responsive promoter comprises a polynucleotide that has a regulatory region of the heat shock genes given in the specification, that has an RpoH recognition site, or that is at least 75% identical to a polynucleotide comprising 55, 62, 63 (2 sequences), 64 (9 sequences), 65 (7 sequences), or 66 bp fully defined in the specification. The solubility responsive promoter is upregulated or downregulated when the target polypeptide is expressed in insoluble form. The polynucleotide that encodes the target polypeptide is heterologous to the host cell. The target protein-expressing nucleic acid comprises a promoter operably linked to the polynucleotide that encodes the target polypeptide or that is heterologous to the host cell or to the polynucleotide that encodes the target polypeptide. The protein solubility responsive promoter is a prokaryotic promoter or a Gram negative bacterial promoter. The Gram negative bacterium is a member of the family Enterobacteriaceae which consists of the genera Salmonella, Shigella, Klebsiella, Enterobacter, or preferably Escherichia coli. The protein solubility responsive promoter may also be a Gram positive bacterial promoter or a eukaryotic promoter. The promoter is a mammalian, plant, insect, fungal, or yeast promoter. The reporter gene comprises a polynucleotide that encodes a selectable or detectable polypeptide such as a metabolic enzyme, antibiotic resistance factor, a chemiluminiscent protein, or a fluorescent protein. The detectable polypeptide is beta-galactosidase, a luminiscent or fluorescent protein. The reporter gene further comprises a polynucleotide that encodes a signal peptide that directs the detectable polypeptide to a surface of the host cell.

The host cell further comprises a molecular **tag** that facilitates separation of a host cell that expresses the reporter gene from a host cell that does not express the reporter gene. The protein solubility responsive promoter is from the same species as is the host cell. The target polypeptide comprises a fragment of a larger polypeptide or a mutated form of a polypeptide, where the fragment comprises a domain of the larger polypeptide. This domain is identified by homology to other polypeptides, by hydropathy plot, or both. The above fragment comprises a polypeptide encoded by a random fragment of a polynucleotide that encodes the larger polypeptide. Preferred Method: The expression of the reporter gene is determined by performing a quantitative assay to determine the amount of detectable or selectable polypeptide in the cell. The host cells are subjected to sorting, in order to separate cells having increased or decreased expression of the reporter gene from cells in which expression of the target polypeptide does not change the expression level of the reporter gene. The cell sorting comprises fluorescence activated cell sorting. The solubility reporter nucleic acid further comprises a polynucleotide that encodes a molecular **tag**, and a polynucleotide that encodes a signal peptide, where the signal polypeptide, the molecular **tag**, and a detectable or selectable polypeptide encoded by the reporter gene are expressed as a fusion protein and the signal polypeptide directs the detectable or selectable polypeptide to a surface of the cell. The method (2) further comprises contacting host cells with a solid support to which the molecular **tag** can bind, where cells that express the reporter gene are immobilized on the solid support. The molecular **tag** comprises an epitope for an antibody, a poly-histidine **tag**, or a FLAG peptide. This method further comprises lysing the host cells under non-denaturing conditions after expressing the target polypeptide, where the target polypeptide is in a liquid phase if expressed in soluble form, and in a solid phase if expressed in insoluble form, and determining the amount of soluble target polypeptide in the liquid phase. The method may also comprise removing an aliquot of the liquid phase after lysing the cells, and contacting the polypeptide with a detection reagent that binds to the molecular **tag** to determine the amount of soluble target polypeptide in the liquid phase. The aliquot is placed on a solid support to which the target polypeptide binds prior to contacting the polypeptide with the detection reagent. The solid support is composed of glasses, plastics, polymers, metals, metalloids, ceramics, or organics. It comprises a microtiter plate, a nitrocellulose membrane, a nylon membrane, a derivatized nylon membrane, or an agarose particle. The cell employed in the method of identifying mutations in a cell that alter the solubility of a target polypeptide, is treated with the mutagen after introducing either or both of the solubility reporter nucleic acid and the target polypeptide-expressing nucleic acid into the cell. The solubility is altered to enhance or decrease solubility. In identifying variations in a process for biosynthesis of a target polypeptide, at least 2 cells are cultured and the expression of the reporter gene in each cell, is compared, thus identifying a cell that expresses an altered

amount of soluble target polypeptide. The protein solubility responsive promoter is upregulated if the target polypeptide is expressed in insoluble form, and expression of the reporter gene at a lower level is indicative of a process or condition that results in greater expression of soluble target polypeptide. In screening an expression library, the protein solubility responsive promoter is upregulated or downregulated when the target polypeptide is expressed in insoluble form, and host cells that express soluble target polypeptide express the reporter gene at a decreased or increased level, respectively, compared to host cells that express insoluble target polypeptides. In identifying a promoter, the putative protein solubility responsive promoter is a heat shock promoter, a eukaryotic promoter or a prokaryotic promoter. Preferred **Array**: The target polypeptides in the **array** differ due to amino acid substitutions, deletions, or insertions compared to a reference amino acid sequence.

USE - The host cells are useful in monitoring the solubility of a target protein in a cell and in identifying mutations in the cell or in the polynucleotide encoding the target protein. The methods are useful in identifying variations in a protein biosynthetic process that alters the solubility of a target protein, in screening an expression library of recombinant clones that express soluble proteins, and in identifying an antibiotic agent.

EXAMPLE - No suitable example given.(69 pages)

L12 ANSWER 4 OF 6 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-10386 BIOTECHDS
TITLE: Determining target nucleic acid sequence useful for diagnosing genetic disease or chromosomal abnormality, comprises determining identity of polypeptide encoded by nucleic acid by using mass spectrometry technique; DNA sequence detection for tagged protein characterization and disease diagnosis
AUTHOR: LITTLE D; KOESTER H; HIGGINS G S; LOUGH D
PATENT ASSIGNEE: SEQUENOM INC
PATENT INFO: US 6322970 27 Nov 2001
APPLICATION INFO: US 1997-146054 2 Sep 1997
PRIORITY INFO: US 1998-146054 2 Sep 1998
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-170704 [22]
AN 2002-10386 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - New process for determining, (M1), target nucleic acid, (TN), sequence comprises determining identity of polypeptide (P) encoded by TN.

DETAILED DESCRIPTION - Determining, (M1), target nucleic acid (TN) sequence by determining identity of polypeptide (P) encoded by TN involves: (1) preparing encoded (P) from TN by in vitro translation, or by in vitro transcription followed by translation, of TN; (2) determining molecular mass of encoded (P) by mass spectrometry; and (3) determining identity of (P) by comparing molecular mass of (P) with molecular mass of corresponding known (P). An INDEPENDENT CLAIM is also included for a process for obtaining information on sequences of several nucleic acid molecules by determining the identity of several target polypeptides encoded by the nucleic acid molecules involves (M2-M3): (a) carrying out steps: (i) obtaining several nucleic acid molecules encoding several

target polypeptide; (ii) preparing a several differentially mass modified target polypeptides from the several nucleic acid molecules; (iii) determining the molecular mass of each differentially mass modified target polypeptide in the set by mass spectrometry; and (iv) determining the identity of each target polypeptide in the set by comparing the molecular mass of each differentially mass modified target polypeptide in the set with molecular mass of a corresponding known polypeptide, thereby obtaining information on several nucleotide sequences encoding the target polypeptides, where each encoded polypeptide is immobilized on the solid support through a cleavable linker; and (b) carrying out steps: (i) ; and (ii) as described for (M2); (iii) contacting each of the encoded polypeptide with at least one agent that cleaves at least one peptide bond in each encoded polypeptide to produce peptide fragments of each encoded polypeptide; (iv) determining the molecular mass of at least one of the peptide fragments of each encoded **polypeptide** in the **plurality** by mass spectrometry; and (v) determining the identity of the each encoded **polypeptide** in the **plurality** by comparing the molecular mass of peptide fragments of each encoded polypeptide with the molecular mass of peptide fragments of a corresponding known polypeptide.

WIDER DISCLOSURE - Kits containing components useful for determining the identity of target polypeptide based on (M1), is also disclosed.

BIOTECHNOLOGY - Preferred Method: In (M1), preferably, sequence information of TN, preferably an RNA molecule, is obtained by determining the identity of the encoded polypeptide which is obtained by in vitro translation, performed in a eukaryotic cell-free extract such as reticulocyte lysate and/or wheat germ extract. The RNA is prepared by in vitro transcription of TN. The in vitro transcription is performed in a cell-free extract (reticulocyte lysate or Escherichia coli S30 cell-free extract), and the translation of the RNA is performed in the same cell-free extract. Optionally, the transcription the transcription or translation is performed in vivo in a host bacterial cell. The encoded polypeptide obtained after the translation process is isolated prior to mass spectrometry by reaction with an antibody. Prior to determining the molecular mass by mass spectrometry, the target polypeptide is immobilized on a solid support: (a) through a cleavable linker (CL) such as an acid cleavable linker, acid-labile linker, heat sensitive linker or a photocleavable linker; (b) by interacting specifically with a polypeptide that is conjugated to a solid support which has a flat surface or has a surface with a structure; or (c) by hydrophobic interaction, hydrophilic interaction, or ionic interaction Optionally, the target polypeptide may be covalently conjugated to the solid support by reaction with a thiol-reactive functionality. The target polypeptide is linked to the solid support by its N-terminal or C-terminal amino acid. The solid support is a bead, bead in an **array** of pits, a capillaries, a flat support, a plastic material, a wafer, a comb, a pin, or **array** of pins, a needle, a **array** of needles, well or nanoliter wells. The beads are silica gel beads, controlled pore glass beads, magnetic beads, 4-(hydroxymethyl)phenoxymethylcopoly(styrene-1% divinylbenzene) resin, chloromethylated copolystyrene-divinylbenzene resin, cellulose beads, agarose beads or dextran beads. The flat supports

are preferably glass fiber filters, glass surfaces, or metal (steel, gold, silver, aluminum, silicon or copper) surfaces. The plastic materials are polyethylene, polypropylene, polyamide, or polyvinylidene difluoride. The wafers are silicon wafers, wafers with pits, wafers with or without filter bottoms. The method further involves amplifying TN using: (i) a forward primer and a reverse primer; (ii) a primer comprising a nucleotide sequence encoding a regulatory element (RE) such as a ribosome binding site, a START codon or a transcription start signal, where following amplification the regulatory element is operably linked to the nucleic acid encoding the encoded polypeptide; (iii) a primer comprising a nucleotide sequence encoding an RNA polymerase promoter (SP6 promoter, T3 promoter, and T7 promoter), where following amplification the promoter is operably linked to TN. TN further comprises an operably linked exogenous nucleotide sequence encoding an RE, and a nucleotide sequence or its complement encoding a second polypeptide which is a **tag** peptide such as myc epitope, Haemophilus influenzae hemagglutinin peptide, polyhistidine sequence, polylysine sequence, polyarginine sequence or glutathione-S-transferase (GST). Optionally, the polypeptide encoded by TN comprises a **tag** biotin or its derivative) that is conjugated to the polypeptide. In this case the polypeptide after translation is isolated by reaction with an agent that specifically interacts with the **tag**, a **tag** peptide with a reagent such as an antibody. Alternately, the **tag** is: (i) a polyhistidine **tag** peptide, and the reagent is a metal ion such as nickel or cobalt ion; or (ii) a polylysine or polyarginine **tag** peptide, which interacts with a reagent such as copper ion or zinc ion that is chelated to a solid support. If the **tag** is biotin or its derivative, the polypeptide is isolated by interaction with avidin or streptavidin. The molecular mass of polypeptide encoded by TN is determined by mass spectrometry technique such as matrix assisted laser desorption ionization (MALDI), delayed extraction MALDI, continuous or pulsed electrospray, ionspray, thermospray, or massive cluster impact and a detection format such as linear time-of-flight, reflectron time-of-flight, single quadrupole, multiple quadrupole, single magnetic sector, multiple magnetic sector, Fourier transform ion cyclotron resonance and/or ion trap. Preferably, the mass is determined by matrix-assisted laser desorption/ionization time-of-flight spectrometry. In (M2), the target polypeptide is obtained by in vitro translation, or by in vitro transcription followed by translation of TN. Prior to step (iii), each encoded polypeptide is immobilized on a solid support and is conditioned by anion exchange, cation exchange, treatment with an alkylating agent, treatment with trialkylsilylchloride or incorporation of modified amino acids. The encoded polypeptide is immobilized: (a) to solid support by CL to a solid support which has a flat surface or has a surface with a structure; or (b) in an **array** to the solid support; or (c) due to interaction with the polypeptide of interest, where the polypeptide of interest is conjugated in an **array** to the solid support.In (M3), each of the encoded polypeptide is immobilized to a solid support prior to contacting each polypeptide with the agent which is an endopeptidase. The encoded polypeptide is preferably immobilized to a solid support through a chemically cleavable linker at one terminus of the polypeptide and through a photocleavable linker at the other terminus of the polypeptide. Preferably, the encoded polypeptides are immobilized in an **array**. Each encoded

polypeptide is mass modified, conditioned prior to step (iii), or the at least one peptide fragment of each of encoded polypeptide is mass modified, conditioned prior to step (iv). The conditioning is carried out as described above.

USE - Obtaining information on a sequence of target nucleic acid molecule by determining identity of a polypeptide encoded by a nucleic acid molecule. The target nucleic acid encoding a polypeptide may be an allelic variant of a polymorphic region of a gene (e.g., BRCA11, BRCA2, APC, dystrophin gene, beta-globin, Factor IX, factor VIIc, ornithine-d-amino-transferase, hypoxanthine guanine phosphoribosyl transferase, cystic fibrosis transmembrane conductance regulator (CFTR), p53, or a proto-oncogene) of a subject, or an allelic variant of a polymorphic region that is located in a chromosomal region that is not in a gene (e.g., a mitochondrial gene). The polymorphic region (e.g., major histocompatibility complex) may be associated with graft rejection, and the novel method in this case is useful for determining compatibility between a donor and recipient of a graft. The allelic variant which is due to a point mutation may be associated with a disease or condition, thereby indicating that a subject has or is at risk of developing a disease or condition. The disease or condition can be associated with an abnormal number of nucleotide repeats (trinucleotide repeats) in the allelic variant, e.g., Huntington's disease, prostate cancer, Fragile X syndrome type A, myotonic dystrophy type I, Kennedy disease, Machodo-Joseph disease, denatorubral and pallidolyusian atrophy, spino bulbar muscular atrophy or aging. The target nucleic acid optionally may comprise nucleotide repeats and the novel method is used for genotyping the subject, forensic analysis and paternity testing. The genotyping is performed by quantifying the number of nucleotide repeats which may be dinucleotide, trinucleotide, tetranucleotide, or pentanucleotide repeats.

The method is useful for obtaining sequence information of a target nucleic acid obtained from an infectious organism such as virus, bacterium, fungus or a protist. (M1) is useful for identifying a target nucleic acid molecule by determining the identity of a polypeptide encoded by the nucleic acid molecule. The method involves preparing the encoded polypeptide by in vitro transcription followed by translation, of a target nucleic acid molecule encoding the polypeptide; contacting the encoded polypeptide with at least one agent that cleaves at least one peptide bond in the encoded polypeptide to produce peptide fragments of the encoded polypeptide; determining the molecular mass of at least one of the peptide fragments of the encoded polypeptide by mass spectrometry; and comparing the molecular mass of the peptide fragments of the encoded polypeptide with the molecular mass of peptide fragments of a corresponding known polypeptide, thereby determining the identity of the encoded polypeptide and the target nucleic acid molecule. The encoded polypeptide is immobilized to a solid support prior to contacting the encoded polypeptide with the agent (preferably, an endopeptidase), through a cleavable linker. Preferably, the encoded polypeptide is immobilized to a solid support through a chemically cleavable linker at one terminus of the polypeptide and through a photocleavable linker at the other terminus of the polypeptide. The encoded polypeptide or its fragments is conditioned prior to step (iii) or the fragments of the encoded polypeptide are conditioned prior to step (iv). The conditioning is by anion exchange, cation exchange, treatment with an alkylating agent, treatment with trialkylsilylchloride or incorporation of modified amino acids (all claimed). (M1) can also be used for diagnosing a genetic

disease or chromosomal abnormality; a predisposition to or an early indication of a gene influenced disease or condition, e.g., obesity, atherosclerosis, diabetes, or cancer; or an infection by a pathogenic organism, e.g., virus, bacterium, parasite or fungus; or to provide information relating to identity, heredity or compatibility using mini-satellite or micro-satellite sequences for human leukocyte antigen (HLA) phenotyping. The methods are also useful for identifying mutations, and thus for screening genetic disorders.

ADVANTAGE - The method is fast, reliable, for indirectly obtaining nucleic acid sequence information. Mass spectrometric detection of polypeptides yields analytical signals of far higher sensitivity and resolution than signals routinely obtained with DNA due to the inherent instability of DNA to volatilization and its affinity for non-volatile cationic impurities.

EXAMPLE - Genomic DNA was obtained from 4 patients having spino-cerebellar ataxia (SCA)-1. A region of the extracted DNA containing the (CAG) repeat associated with SCA-1 was amplified by PCR using primers modified to contain a transcription promoter sequence and a region coding for a His-6 **tag** peptide. The forward primer was 5'-d(GACTTTACTTGTACGTGCATAATACGACTCACTATAGGGAGACTGAC CATGGGCAGTCTGAGCCA). The reverse primer encoding the His-6 **tag** peptide was 5'-d(TGATTCTCAATGATGATGATGATGATGAAATTGAAATGTGGACGTAC). Coupled transcription and translation was performed using the TNT reaction buffer. The translated His-6 tagged polypeptide was purified. The translated polypeptide was mixed with matrix either directly from the elution solution or first was lyophilized and resuspended in 5 mul H2O. This solution was mixed 1:1 (v:v) with matrix solution and 0.5 mul of the mixture was added to a sample probe for analysis in a linear time-of-flight mass spectrometer operated in delayed ion extraction mode with a source potential of 25 kV. Internal calibration was achieved for all spectra using three intense matrix ion signals. Three of the patients had 10, 15, or 16 CAG repeats and the fourth patient had an unknown number of trinucleotide repeats. Mass spectrometric analysis of the peptides encoded by target polypeptides encoded by the 10, 15, and 16 CAG repeats indicated that these peptides had a molecular mass of 8238.8, 8865.4, and 8993.6 Daltons, respectively. The polypeptide encoded by the nucleic acid from the fourth patient, having an unknown number of trinucleotide repeats had a molecular weight of 8224.8 Da. This value did not correspond exactly with a unit number of repeats (10 was the closest), but consistent with detection of a point mutation; i.e., the -14 Dalton shift for this polypeptide corresponded to an Ala-Gly mutation due to a C-G mutation in one of the repeats. (50 pages)

L12 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:377043 CAPLUS
DOCUMENT NUMBER: 138:381721
TITLE: Methods for preparing a simple system for storage and/or delivery of oligomer and/or a polymer applied to supports without contamination and degradation
INVENTOR(S): Hayashizaki, Yoshihide

PATENT ASSIGNEE(S): Riken Corp., Japan; Kabushiki Kaisha Dnaform
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040360	A1	20030515	WO 2002-JP11492	20021105

W: CA, JP, US
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR
PRIORITY APPLN. INFO.: JP 2001-339217 A 20011105
AB A method for storing and/or delivering an oligomer and/or polymer applied on at least one support, comprising the steps of:(a) applying at least one oligomer and/or polymer on at least one support; (b) folding or rolling the support; and(c) storing and/or delivering the support of step (b)is provided. Also, a support having at least one oligomer and/or polymer applied thereon, which is in the form of a folded or rolled sheet, a loose-leaf sheet or a card and a water-sol. support having at least one oligomer and/or polymer applied thereon are provided. According to the present invention, mol. substances (oligomers and/or polymers) can be stored and delivered in a simple system. This system can preserve the substances without contamination and degrdn. The oligomers and/or polymers include oligonucleotide, oligopeptide, oligosaccharide, PNA, polynucletide, **polypeptide**, polysaccharide and a **mixt**.
thereof. The supports made of a water-sol., water-dissolvable and/or water-insol. material. The support is inserted in a container which is an envelope, a bag, a can, a box, a jar, an ampulle or a tube. The soln. of the oligomer and/or polymer directly to the support by a pin, syringe or ink-jet printer.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:575354 CAPLUS
DOCUMENT NUMBER: 137:104764
TITLE: Nucleic-acid programmable protein arrays
INVENTOR(S): Labaer, Joshua; Lau, Albert Y.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059601	A1	20020801	WO 2002-US1882	20020122

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,

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            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
            TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    US 2002192673     A1   20021219       US 2002-55432    20020122
PRIORITY APPLN. INFO.:                  US 2001-263607P  P  20010123
AB  Arrays of polypeptides are generated by translation of nucleic acid
    sequences encoding the polypeptides at a plurality of
    addresses on the array.
REFERENCE COUNT:          5     THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT


=> d his

     (FILE 'HOME' ENTERED AT 17:40:02 ON 26 JUN 2003)

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 17:40:16 ON 26 JUN 2003
L1          2293 S CHRISTIANS F?/AU OR COLE K?/AU
L2           197 S OLIGO TAG# OR NUCLEIC ACID TAG# OR OLIGONUCLEOTIDE TAG#
L3             0 S L1 AND (SCREEN### (4A) POLPEPTIDE#)
L4             1 S L1 AND L2
L5             0 S (SCREEN### (4A) POLPEPTIDE#)
L6          1884 S (SCREEN### (4A) POLYPEPTIDE#)
L7             2 S L6 AND L2
L8        319682 S PROBE ARRAY OR ARRAY OR MICROARRAY OR GENECHIP OR GENFLEX
ARR
L9          2795 S ((PLURALITY OR MULTIPLE OR MIXTURE) (4A) POLYPEPTIDE#)
L10           56 S L9 AND L8
L11            0 S L10 AND L2
L12            6 S L10 AND TAG

=> s l9 and tag
L13           25 L9 AND TAG

=> s l13 and l8
L14            6 L13 AND L8

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     (FILE 'HOME' ENTERED AT 17:40:02 ON 26 JUN 2003)

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 17:40:16 ON 26 JUN 2003
L1          2293 S CHRISTIANS F?/AU OR COLE K?/AU
L2           197 S OLIGO TAG# OR NUCLEIC ACID TAG# OR OLIGONUCLEOTIDE TAG#
L3             0 S L1 AND (SCREEN### (4A) POLPEPTIDE#)
L4             1 S L1 AND L2
L5             0 S (SCREEN### (4A) POLPEPTIDE#)
L6          1884 S (SCREEN### (4A) POLYPEPTIDE#)
L7             2 S L6 AND L2
L8        319682 S PROBE ARRAY OR ARRAY OR MICROARRAY OR GENECHIP OR GENFLEX
ARR
L9          2795 S ((PLURALITY OR MULTIPLE OR MIXTURE) (4A) POLYPEPTIDE#)
L10           56 S L9 AND L8
L11            0 S L10 AND L2
L12            6 S L10 AND TAG
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L13          25 S L9 AND TAG
L14           6 S L13 AND L8

=> s l8 and l6
L15         228 L8 AND L6

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L16          14 L15 AND TAG

=> dup rem l16
PROCESSING COMPLETED FOR L16
L17          10 DUP REM L16 (4 DUPLICATES REMOVED)

=> d ibib abs l17 1-10

L17   ANSWER 1 OF 10  BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2003-10989  BIOTECHDS
TITLE:            Identifying an agent that modulates ChemR23 polypeptide
using
                  TIG2 gene, useful for the preparation of a medicament for
the
                  treatment of disorders, such as cancer, inflammatory and
                  autoimmune diseases, osteoporosis and psoriasis;
                     protein receptor modulation, antibody and transgenic
                     animal model for use in gene therapy
AUTHOR:           WITTAMER V; COMMUNI D; VANDENBOGAERDE A; DETHEUX M;
                  PARMENTIER M
PATENT ASSIGNEE:  EUROSCREEN SA
PATENT INFO:      WO 20030006996 23 Jan 2003
APPLICATION INFO: WO 2002-EP7647 9 Jul 2002
PRIORITY INFO:    US 2001-905253 13 Jul 2001; US 2001-303858 9 Jul 2001
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2003-221782 [21]
AN    2003-10989  BIOTECHDS
AB    DERWENT ABSTRACT:
      NOVELTY - Identifying an agent that modulates the function of an orphan
      G-protein coupled receptor, ChemR23, is new.
           DETAILED DESCRIPTION - Identifying an agent that modulates the
      function of an orphan G-protein coupled receptor, ChemR23, comprises
      contacting a ChemR23 polypeptide with a tazarotene-induced gene 2 (TIG2)
      polypeptide in the presence and absence of a candidate modulator to
      permit the binding of the TIG2 polypeptide to the ChemR23 polypeptide,
      and measuring the binding of the ChemR23 to the TIG2 polypeptide, where
a
      decrease in the presence of the candidate modulator, identifies the
      modulator as an agent that modulates the function of ChemR23. The method
      further comprises contacting a ChemR23 polypeptide with a candidate
      modulator, measuring a signaling activity of the ChemR23 polypeptide,
      where a change in the activity in the presence of the candidate
modulator
      relative to the activity in the absence of the candidate modulator
      identifies it as an agent that modulates the function of ChemR23, and/or
      comparing the activity measured in the presence of the candidate
      modulator to the activity measured in a sample in which the ChemR23
      polypeptide is contacted with a TIG2 polypeptide at its EC50, where the
      candidate modulator is identified as an agent that modulates function of
      ChemR23 when the amount of the activity measured in the presence of the
      candidate modulator is at least 50% of the amount induced by the TIG2
      polypeptide present at EC50. INDEPENDENT CLAIMS are also included for
the
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following: (1) detecting the presence, in a sample, of an agent that modulates the function of ChemR23 in a sample, comprising contacting a ChemR23 polypeptide with a TIG2 polypeptide in the presence and absence of the sample to permit the binding of the TIG2 polypeptide to the ChemR23 polypeptide, and measuring the binding of the ChemR23 to the TIG2 polypeptide, where a decrease in the presence of the sample, identifies the presence of an agent that modulates the function of ChemR23 in the sample, and /or contacting a ChemR23 polypeptide with a sample, measuring a signaling activity of the ChemR23 polypeptide, where a change in the activity in the presence of the sample relative to the activity in the absence of the sample identifies an agent that modulates the function of ChemR23, and/or comparing the activity measured in a reaction containing ChemR23 and TIG2 polypeptides without the sample to the activity measured with a sample in which the ChemR23 polypeptide is contacted with a TIG2 polypeptide at its EC50, where the sample is identified as containing an agent that modulates function of ChemR23 when the amount of the activity measured in the presence of the sample is at least 50% of the amount induced by the TIG2 polypeptide present at EC50; (2) modulating the activity of a ChemR23 polypeptide in a cell, comprising delivering an agent that modulates the activity of ChemR23 polypeptide to the cell; (3) an agent identified by any of the methods cited above; (4) a composition comprising the agent of (3); (5) a truncated TIG2 peptide comprising any of 12 fully defined sequences of 151-162 amino acids, given in the specification; (6) a nucleotide sequence encoding the truncated TIG2 peptide, comprising a fully defined sequence of 471 bp, given in the specification; (7) diagnosing a disease or disorder with dysregulation of ChemR23 signaling, comprising contacting a tissue sample with an antibody specific for a ChemR23 and/or TIG2 polypeptide, detecting binding of the antibody to the tissue sample, and comparing the binding detected with a standard, where a difference in binding relative to the standard is diagnostic of a disease or disorder with dysregulation of ChemR23, or isolating nucleic acid from a tissue sample, amplifying a ChemR23 or TIG2 polynucleotide, using the nucleic acid as a template, and comparing the amount or sequence of amplified ChemR23 or TIG2 polynucleotide produced with a standard, where a difference in the amount or sequence of amplified ChemR23 or TIG2 polynucleotide relative to the standard is diagnostic of a disease or disorder; (8) a composition comprising an isolated ChemR23 or TIG2 polypeptide;(9) an antibody specific for a ChemR23 or TIG2 **polypeptide**; (10) a kit for **screening** for agents that modulate the signaling activity of ChemR23, comprising an isolated ChemR23 polypeptide, an isolated polynucleotide encoding a ChemR23 polypeptide or, a cell transformed with a polynucleotide encoding a ChemR23 polypeptide, and packaging materials; (11) a kit for the diagnosis of a disease or disorder with dysregulation of ChemR23, comprising an isolated ChemR23 polypeptide, an isolated polynucleotide encoding a ChemR23 polypeptide or, a cell transformed with a polynucleotide encoding a ChemR23 polypeptide, and packaging materials; and (12) a non-human mammal having a homozygous null mutation in the gene encoding ChemR23, or that is transgenic for a ChemR23 or TIG2 polynucleotide.

BIOTECHNOLOGY - Preferred Method: The TIG2 polypeptide in the method of identifying an agent that modulates ChemR23 is detectably labeled, preferably with a moiety that is a radioisotope, a fluorophore, a quencher of fluorescence, an enzyme, an affinity **tag** or an epitope **tag**. The contacting is performed in or on a cell expressing the ChemR23 polypeptide, or on synthetic liposomes, or on virus-induced budding membranes containing a ChemR23 polypeptide. The method is performed using a membrane fraction from cells expressing a ChemR23 polypeptide. The measuring is performed using label displacement, surface plasmon resonance, fluorescence resonance energy transfer, fluorescence quenching or fluorescence polarization. The agent is a peptide, polypeptide, antibody or antigen-binding fragment, a lipid, carbohydrate, nucleic acid or a small organic molecule. The step of measuring a signaling activity comprises detecting a change in the level of a second messenger, or comprises measurement of guanine nucleotide binding or exchange, adenylate cyclase activity, cAMP, protein kinase C activity, phosphatidylinositol breakdown, diacylglycerol, inositol triphosphates, intracellular calcium, arachinoid acid, MAP kinase activity, tyrosine kinase activity or reporter gene expression, and preferably using an aequorin-based assay. The TIG2 polypeptide has at least 31% identity or higher, such as 45%, 55%, 65%, 75%, 85%, 95% or 100% to a fully defined sequence of 163 amino acids (S1), and where it binds specifically to and activates a signaling activity of a ChemR23 polypeptide with a fully defined sequence of 376 amino acids (S2), all given in the specification. The TIG2 polypeptide further comprises one or more additions, insertions, deletions or substitutions relative to (S2). Alternatively, the TIG2 polypeptide is a truncated TIG2 polypeptide with any of 12 fully defined sequences of 151-162 amino acids, given in the specification. The polypeptide additionally comprises additional sequences forming a TIG2 fusion protein. The additional sequences are glutathione-S-transferase, maltose binding protein, alkaline phosphatase, thioredoxin, green fluorescent protein, histidine tags or epitope tags. The standard in the method of (7) is a fully defined sequence of 1290 bp, given in the specification. The step of comparing the sequence comprises missequencing, where the standard is a fully defined sequence of 588 bp, given in the specification. The comparing of amount or sequence is performed on a **microarray**.

ACTIVITY - Cytostatic; Antiinflammatory; Immunosuppressive; Osteopathic; Antipsoriatic; Dermatological; Antibacterial; Virucide; Antihelmintic; Gynecological. No biological is data given.

MECHANISM OF ACTION - G-Protein-Agonist; G-Protein-Antagonist; Gene-Therapy.

USE - The agent or composition is useful for the preparation of a medicament for the treatment of a ChemR23- or TIG2-related disease or disorder, such as cancer, tumor metastasis, inflammatory disease, autoimmune disease, inherited or acquired immune deficiencies, osteoporosis, bone healing, bone tissue grafts, graft rejection, psoriasis, eczema, inflammatory infection, trophic diseases of skin, viral, bacterial and parasitic infections, female infertility and ovarian and uterine tumors. The truncated or full-length TIG2 polypeptide is useful for the production of a composition of an isolated ChemR23 or TIG2 polypeptide, and/or for the production of a kit for screening agents that

modulate the signaling of ChemR23, and/or ligand for ChemR23 (all claimed).

EXAMPLE - No suitable example is given.(99 pages)

L17 ANSWER 2 OF 10 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2003-10485 BIOTECHDS
TITLE: New nucleic acid sequence comprising an ANGE, CLLD8 or CLLD7 mRNA, or their hybrid, useful for screening agents for treating IgE-mediated diseases, e.g. asthma, atopy, hay fever, eczema, atopic dermatitis, or allergic rhinitis; recombinant protein production and antibody for use in disease therapy and gene therapy
AUTHOR: ZHANG Y; MOFFATT M; COOKSON W; TINSLEY J
PATENT ASSIGNEE: ISIS INNOVATIONS LTD
PATENT INFO: WO 20030000727 3 Jan 2003
APPLICATION INFO: WO 2002-GB2859 21 Jun 2002
PRIORITY INFO: GB 2001-15213 21 Jun 2001; GB 2001-15211 21 Jun 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-201405 [19]
AN 2003-10485 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Isolated or recombinant nucleic acid (I) sequence comprising an ANGE, CLLD8 or CLLD7 mRNA, or ANGE-CLLD8, ANGE-CLLD7, CLLD7-CLLD8, or ANGE-CLLD8-CLLD7 hybrid mRNA sequence, its complement, homologue or fragment, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) isolated recombinant nucleic acid sequence comprising a single nucleotide polymorphism in (I); (2) isolated or recombinant nucleic acid sequence that hybridizes to (I) under stringent conditions; (3) primer sequence fully disclosed in the specification; (4) vector comprising any of the nucleic acid sequences cited above; (5) polypeptide sequence encoded by (I); (6) antibody specific for, or reacts with the polypeptide or any of the nucleic acid sequences cited above; (7) preparing any of the nucleic acid sequence by ligating together successive nucleotide and/or oligonucleotide residues; (8) preparing the polypeptide by ligating together successive amino acids and/or oligopeptide residues; (9) host cell comprising the vector; (10) transgenic non-human animal comprising the vector or any of the nucleic acid sequences cited above, which results in disease, or that does not substantially express the above sequences; (11) diagnosing, determining predisposition to, or susceptibility of a subject to atopy or disease, or predicting the severity of the disease in an individual; (12) diagnosing an individual as being atopic or having abnormal serum IgE levels or an STI above 5mm; (13) splice variant of ANGE, CLLD8, or CLLD7 for diagnosing an IgE-mediated disease, atopy, a form of atopic disease or non-atopic asthma, or predicting the severity, or predisposition to a disease; (14) kit comprising the splice variant cited above, or for diagnosing of, or predisposition to the disease comprising means for determining the presence or absence of a risk allele that is diagnostic of, or predisposition to, or severity of the disease; (15) identifying a compound for treating a disease; (16) agent or antibody for treating IgE-mediated diseases, such as asthma, atopy, hay fever, eczema, atopic dermatitis, allergic rhinitis or non-atopic asthma; (17) pharmaceutical composition comprising the nucleic acid, polypeptide or antibody; (18) preventing or treating disease in a subject; (19) agent capable of influencing expression of the ANGE, CLLD8, or CLLD7 gene; and (20) a

screen for identifying an agent that modulates the activity of the ANGE, CLLD7 or CLLD8 gene, or any combination of one or more of these genes or any splice variant, or a screen for detecting the side effect of such agent.

BIOTECHNOLOGY - Preferred Sequence: The recombinant nucleic acid comprises a sequence that encodes a human or mouse polypeptide, its complement, homologue or fragment. The ANGE nucleic acids comprise one or more exons of ANGE 1, its complement, homologue or fragment. The nucleic acid sequence in (1) comprises part of a fully defined sequence of 410847 base pair (bp) (S1), given in the specification having one or more SNPs at positions corresponding to the sequence. The nucleic acid sequence in (2) is capable of distinguishing between alleles of a SNP given in the specification. The polypeptide sequence is operably linked to a secretion signal, and comprises a histidine **tag**. It is also linked to a carrier. Preferred Antibody: The antibody is a chimeric, humanized or bifunctional antibody. Preferred Method: In preparing the polypeptide, the polypeptide is produced in a cell-free system. Diagnosing or determining predisposition or susceptibility of a subject to atopy or predicting severity of disease in an individual comprises determining the presence of a variant form of the ANGE, CLLD7, or CLLD8 gene, their combinations or splice variants of the gene. Diagnosing an individual as being atopic comprises demonstrating in an individual the presence or absence of an allele that is associated with one or more of the SNP markers and optionally any other SNP in linkage disequilibrium with the markers. The allele can be associated with the haplotype 18575b4-2, 185752b5-3 or 4321017b38-1. Diagnosing or determining predisposition to disease comprises determining the presence or absence of an allele of SNP marker at position 18575b4-2, 185752b5-3 or 4321017b38-1, where the presence of the allele is a diagnostic of disease or predisposition to a disease. Diagnosing an individual as having abnormal serum IgE levels comprises determining in an individual the presence or absence of an allele that is associated with the SNP marker 185752b4-2 and optionally any other SNP in linkage disequilibrium with the marker. Diagnosing an individual as having an STI above 5mm comprises determining in an individual the presence or absence of an allele that is associated with the SNP marker 4321017b38-1 and optionally any other SNP in linkage disequilibrium with the marker. The diagnosing methods further comprise providing a suitable sample from the individual, preparing nucleic acid from the sample, and analyzing the nucleic acid sample for the presence or absence of the allele. Prior to the analysis, the region comprising the SNP marker is amplified. These methods comprise the use of a pair of primers that hybridizes under stringent conditions to a region of either side of the SNP. The primers include an oligonucleotide sequence listed in the specification. Identifying a compound for treating a disease comprises administering a compound comprising (I), and determining whether the compound modulates downstream effects of the SNP. Preventing or treating a disease in a subject comprises modulating the activity, expression, half life or post translational modification of ANGE, CLLD7 and/or CLLD8, or any combination of one or more genes or any splice variant of the genes in the subject. The disease is an IgE-mediated disease. This method comprises administering to the subject an agent that is capable of modulating the effects of the disease causing alleles. Identifying an agent that modulates the activity of the ANGE, CLLD7 or CLLD8 gene, or any combination of one or more of these genes or any

splice variant comprises providing the polypeptide sequence cited above, providing a substrate, providing an agent to be tested, and measuring whether the agent to be tested modulates the activity of the polypeptide by measuring processing of the substrate. Alternatively, this method comprises providing the polypeptide, providing an agent to be tested, providing a cell, and measuring whether the agent to be tested modulates the activity of the polypeptide by measuring adhesion of the cell to a surface. The surface can further be a cell, and comprises a biological or non-biological molecule. One or more of the cells are immobilized, which are preferably B-lymphocyte. This cell is a cell transfected with the vector, or the host cell cited above. Moreover, this method comprises providing the polypeptide, providing an agent to be tested, providing a cell, and measuring a change in differentiation or proliferation of the cell. The cell is expressing one or more of the polypeptides cited above.

The change in cellular differentiation involves a change in expression of a cell-signaling factor. The cell-signaling factor is an immunomodulators or a peptide regulatory factor. The cell is cultured following removal from a patient or experimental animal. Furthermore, this screen method can comprise providing a transgenic animal, providing an agent to be tested, contacting the transgenic animal with the agent to be tested, and detecting a change in the transgenic animals phenotype. (I) can also be provided as an alternative to the **polypeptide**, where this **screen** is an in vitro transcription assay measuring the transcription of those genes. Detecting the side effect of the agent identified above comprises providing a cell that does not substantially express the polypeptide sequence, providing an agent to be tested, contacting the agent to be tested with the cell, and measuring any side effect produced by the agent on the cell. The side effect involves a change in cell differentiation or proliferation. The cell is a part of a transgenic animal. The side effect is a measure of the change of phenotype. Preferred Kit: The kit comprising the splice variant preferably comprises two or more splice variants in the form of an **array**, or on a **chip**. Preferred Agent: The agent in (19) is capable of influencing the activity of, or the RNA splicing of the ANGE, CLLD8 or CLLD7 gene, or any combination of two or more gene promoters, or transcripts of the gene.

ACTIVITY - Antiallergic; Antiasthmatic; Dermatological; Antipyretic; Antiinflammatory. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The nucleic acid sequences are useful for screening agents that inhibit or enhances activity of ANGE, CLLD8 or CLLD7 gene. The agent or antibody is useful for treating IgE-mediated diseases, such as asthma, atopy, hay fever, eczema, atopic dermatitis, allergic rhinitis or non-atopic asthma. The antibody is useful in an assay detecting or measuring the polypeptide in the sample. The host cell is useful for producing, regulating and analyzing the polypeptide. The splice variant of ANGE, CLLD8, or CLLD7 is useful for diagnosing an IgE-mediated disease, atopy, a form of atopic disease or non-atopic asthma, or predicting the severity, or predisposition to a disease (all claimed).

ADMINISTRATION - Administration can be oral or parenteral, e.g. topical, intraarterial, subcutaneous, intramedullary, intravenous or intranasal. No dosage is given.

EXAMPLE - Discovery of SNPs was performed through direct sequencing of non-repetitive DNA fragments that were greater than 1000 bp in length.

For each sequence reaction, primers designed covering 500-600 bps genomic sequence. Five individual samples and one pooled DNA panel of 32 individuals were sequenced. Traces were assembled by the Polyphred/Phrap programmes. Following this random SNP discovery, sequencing of all exons with 250 bp leading and trailing DNA was carried out for all potential candidate genes from the region. (429 pages)

L17 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:355701 CAPLUS
DOCUMENT NUMBER: 138:365121
TITLE: Methods for **screening polypeptides** using oligonucleotide tags and immobilization on probe arrays
INVENTOR(S): Christians, Fred; Cole, Kyle B.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 24 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003087232	A1	20030508	US 2002-683613	20020124

PRIORITY APPLN. INFO.: US 2001-264635P P 20010125
AB In one aspect of the invention, methods are provided for the creation and **screening** of **polypeptides** that eliminates bacterial cloning and individual screening. In preferred embodiments, the method involves partnering each protein with a unique DNA oligonucleotide **tag** that directs the protein to a unique site on the **microarray** due to specific hybridization with a complementary **tag**-probe on the **array**.

L17 ANSWER 4 OF 10 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2003-06325 BIOTECHDS
TITLE: Protein **array** used to generate a library of target organism polypeptides;
protein **array** and polymerase chain reaction for protein library construction and vaccine design
AUTHOR: FELGNER P L; DOOLAN D L
PATENT ASSIGNEE: GENE THERAPY SYSTEMS INC
PATENT INFO: WO 2002097051 5 Dec 2002
APPLICATION INFO: WO 2002-US17005 29 May 2002
PRIORITY INFO: US 2001-294739 30 May 2001; US 2001-294739 30 May 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-041408 [03]
AN 2003-06325 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A method for generating a library of target organism polypeptides, is new.

DETAILED DESCRIPTION - A method for generating (I) a library of target organism polypeptides comprising: (a) performing a first PCR reaction using a first primer pair capable of amplifying a desired

polynucleotide sequence form the target organism to provide an amplified coding sequence which amplified coding sequence is not transcriptionally active; (b) providing a second PCR nucleotide primer pair capable of adding at least on e nucleotide sequence that confers transcriptional activity to the amplified coding sequence; (c) performing a second PCR with the second primer pair and the amplified coding sequence thereby resulting in amplification of a transcriptionally active coding sequence;

(d) expressing the polypeptide of the transcriptionally active coding sequence; and (e) repeating steps (a)-(d) at least 10 times with different first primer pairs to express different polypeptides of said target organism.INDEPENDENT CLAIMS are also included for the following: (1) screening (II) a library or target organism polypeptides in order to identify a target organism antigen that is capable of eliciting a humoral immune response: (a) providing a library of target organism polypeptides attached to a linker molecule prepared by (I); (b) immobilizing at least 10 of the target organism polypeptides to a solid support; and (c) assaying the polypeptides with at least one antibody from an animal that has been immunized with one or more antigens from the target organism to identify a target organism antigen capable of eliciting a humoral immune response. (2) screening (III) a library or target organism polypeptides in order to identify a target organism antigen that is capable of eliciting a cell-mediated immune response: (a) providing a library of target organism polypeptides attached to a linker molecule prepared by (I); (b) delivering at least 10 of the target organism polypeptides into a plurality of antigen-presenting cells; and (c) assaying the antigen-presenting cells with at least one T- cell from an animal that has been immunized with one or more antigens from the target organism to identify a target organism antigen capable of eliciting a cell-mediated immune response. (3) developing a subunit vaccine against a target organism; (4) an **array** of at least 20 target organism **polypeptides** prepared by (I); (5) **screening** an **array** in order to identify a target organism antigen; and (6) an automated system capable of performing (I).

BIOTECHNOLOGY - Preferred Method: (I) Steps are repeated at least 266 times. The target organism is vaccinia virus, B. antracis, Francisella tularensis, P. falciparum or Mycobactreium tuberculosis.Further comprises adding at least one polynucleotide operably encoding a linker molecule producing a target organism polypeptide attached to a linker molecule. The linker molecule is an epitope or is selected from 6x, 7x, 8x, 9x and 10x his-**tag**, GST **tag**, fluorescent protein **tag**, Flag **tag** and HA **tag**. At least one sequence that confers transcriptional activity is a promoter or terminator sequence. Designing the first primer pair and the PCR (polymerase chain reaction) is performed using an automated system. (II) and (III) antigen-presenting cells are B cells, macrophages or dendritic cells. The target organism is vaccinia virus. Preferred **Array**: the **array** comprises a plurality of sub arrays and are microtitre plates of 96 wells.

USE - Generating a library of target organism **polypeptides** and **screening** (III) a library or target organism polypeptides in order to identify a target organism (claimed).

EXAMPLE - No suitable example is given in the specification.(60 pages)

L17 ANSWER 5 OF 10 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2003-01246 BIOTECHDS
TITLE: Host cell useful for monitoring the solubility of a target

protein and in identifying mutations in the cell, comprises a
solubility reporter nucleic acid and a target polypeptide-expressing nucleic acid;
vector expression in host cell, DNA library screening for mutation detection and antibiotic agent identification

AUTHOR: LESLEY S; KNUTH M
PATENT ASSIGNEE: IRM LLC
PATENT INFO: WO 2002061041 8 Aug 2002
APPLICATION INFO: WO 2001-US51426 21 Nov 2001
PRIORITY INFO: US 2001-324833 24 Sep 2001; US 2000-721340 21 Nov 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-608512 [65]
AN 2003-01246 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A host cell (I) comprising a solubility reporter nucleic acid with a protein solubility responsive promoter that is operably linked to a reporter gene, and a target polypeptide-expressing nucleic acid that comprises a polynucleotide which encodes a target polypeptide, where an expression of the target polypeptide in an insoluble form causes a change in the expression of the reporter gene, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an **array** of two or more populations of (I), where the host cell of each population differs in the target polypeptides expressed by the host cells; (2) determining the solubility of a target polypeptide, comprising: (a) culturing (I) under conditions in which the target polypeptide is expressed; and (b) determining whether the expression of the reporter gene is increased or decreased, thus, determining the solubility of the expressed target polypeptide; (3) identifying mutations in a cell that alter the solubility of a target polypeptide, comprising: (a) treating a cell with a mutagen; (b) introducing the above solubility reporter nucleic acid and target polypeptide-expressing nucleic acid into the cell; (c) culturing the cell under conditions favorable for expression of the target polypeptide; (d) measuring the expression of the reporter gene; and (e) comparing the level of expression of the reporter gene in the cell with the level observed in an unmutated cell comprising the above nucleic acids to identify a cell that comprises a mutation that alters the solubility of the target polypeptide; (4) identifying alterations to a polynucleotide that encodes a target polypeptide, and which alters the solubility of the target polypeptide, comprising: (a) altering a polynucleotide that encodes the target polypeptide to form an altered polynucleotide; (b) steps (b)-(d) of method (3); and (c) comparing the level of expression of the reporter gene with the level observed in a cell with an unaltered polynucleotide that encodes the target polypeptide, to identify an alteration to the polynucleotide that changes the solubility of the encoded target polypeptide; (5) identifying variations in a process for biosynthesis of a target polypeptide that alters the solubility of the target polypeptide, comprising: (a) culturing (I) under alternative conditions in which the target polypeptide is expressed; and (b) comparing the expression of the reporter gene by host cells grown under each of the alternative conditions; (6) screening an expression library to identify library members that express soluble target polypeptide, comprising: (a) introducing a plurality of expression vectors that

comprise a polynucleotide encoding a target polypeptide into a plurality of (I) to create an expression library; (b) step (a) of method (2); and (c) detecting the expression of the reporter gene, thus, identifying library members that express soluble target polypeptides; (7) identifying an antibiotic agent, comprising: (a) contacting a cell having a solubility reporter nucleic acid with a candidate antibiotic agent, where the nucleic acid comprises a protein solubility responsive promoter operably linked to a reporter gene; and (b) detecting the level of expression of the reporter gene, where a change indicates an agent that inhibits protein folding in the cell; (8) identifying a promoter that is differentially regulated in response to expression of an insoluble polypeptide in a host cell that comprises the promoter, comprising: (a) providing (I); (b) step (a) of method (2); and (c) step (b) of method (2), thus, determining whether the putative protein solubility responsive promoter is differentially regulated in response to expression of an insoluble polypeptide in (I).

BIOTECHNOLOGY - Preferred Host Cell: The host cell comprises a solubility responsive promoter which has a polynucleotide sequence that is at least 75% identical to 9 fully defined sequences comprising 200 bp given in the specification, or to 13 fully defined sequences comprising 300 bp given in the specification. The solubility responsive promoter comprises a polynucleotide that has a regulatory region of the heat shock genes given in the specification, that has an RpoH recognition site, or that is at least 75% identical to a polynucleotide comprising 55, 62, 63 (2 sequences), 64 (9 sequences), 65 (7 sequences), or 66 bp fully defined in the specification. The solubility responsive promoter is upregulated or downregulated when the target polypeptide is expressed in insoluble form. The polynucleotide that encodes the target polypeptide is heterologous to the host cell. The target protein-expressing nucleic acid comprises a promoter operably linked to the polynucleotide that encodes the target polypeptide or that is heterologous to the host cell or to the polynucleotide that encodes the target polypeptide. The protein solubility responsive promoter is a prokaryotic promoter or a Gram negative bacterial promoter. The Gram negative bacterium is a member of the family Enterobacteriaceae which consists of the genera Salmonella, Shigella, Klebsiella, Enterobacter, or preferably Escherichia coli. The protein solubility responsive promoter may also be a Gram positive bacterial promoter or a eukaryotic promoter. The promoter is a mammalian, plant, insect, fungal, or yeast promoter. The reporter gene comprises a polynucleotide that encodes a selectable or detectable polypeptide such as a metabolic enzyme, antibiotic resistance factor, a chemiluminiscent protein, or a fluorescent protein. The detectable polypeptide is beta-galactosidase, a luminiscent or fluorescent protein. The reporter gene further comprises a polynucleotide that encodes a signal peptide that directs the detectable polypeptide to a surface of the host cell. The host cell further comprises a molecular **tag** that facilitates separation of a host cell that expresses the reporter gene from a host cell that does not express the reporter gene. The protein solubility responsive promoter is from the same species as is the host cell. The target polypeptide comprises a fragment of a larger polypeptide or a mutated form of a polypeptide, where the fragment comprises a domain

of the larger polypeptide. This domain is identified by homology to other polypeptides, by hydropathy plot, or both. The above fragment comprises a polypeptide encoded by a random fragment of a polynucleotide that encodes the larger polypeptide. Preferred Method: The expression of the reporter gene is determined by performing a quantitative assay to determine the amount of detectable or selectable polypeptide in the cell. The host cells are subjected to sorting, in order to separate cells having increased or decreased expression of the reporter gene from cells in which expression of the target polypeptide does not change the expression level of the reporter gene. The cell sorting comprises fluorescence activated cell sorting. The solubility reporter nucleic acid further comprises a polynucleotide that encodes a molecular **tag**, and a polynucleotide that encodes a signal peptide, where the signal polypeptide, the molecular **tag**, and a detectable or selectable polypeptide encoded by the reporter gene are expressed as a fusion protein and the signal polypeptide directs the detectable or selectable polypeptide to a surface of the cell. The method (2) further comprises contacting host cells with a solid support to which the molecular **tag** can bind, where cells that express the reporter gene are immobilized on the solid support. The molecular **tag** comprises an epitope for an antibody, a poly-histidine **tag**, or a FLAG peptide. This method further comprises lysing the host cells under non-denaturing conditions after expressing the target polypeptide, where the target polypeptide is in a liquid phase if expressed in soluble form, and in a solid phase if expressed in insoluble form, and determining the amount of soluble target polypeptide in the liquid phase. The method may also comprise removing an aliquot of the liquid phase after lysing the cells, and contacting the polypeptide with a detection reagent that binds to the molecular **tag** to determine the amount of soluble target polypeptide in the liquid phase. The aliquot is placed on a solid support to which the target polypeptide binds prior to contacting the polypeptide with the detection reagent. The solid support is composed of glasses, plastics, polymers, metals, metalloids, ceramics, or organics. It comprises a microtiter plate, a nitrocellulose membrane, a nylon membrane, a derivatized nylon membrane, or an agarose particle. The cell employed in the method of identifying mutations in a cell that alter the solubility of a target polypeptide, is treated with the mutagen after introducing either or both of the solubility reporter nucleic acid and the target polypeptide-expressing nucleic acid into the cell. The solubility is altered to enhance or decrease solubility. In identifying variations in a process for biosynthesis of a target polypeptide, at least 2 cells are cultured and the expression of the reporter gene in each cell, is compared, thus identifying a cell that expresses an altered amount of soluble target polypeptide. The protein solubility responsive promoter is upregulated if the target polypeptide is expressed in insoluble form, and expression of the reporter gene at a lower level is indicative of a process or condition that results in greater expression of soluble target **polypeptide**. In **screening** an expression library, the protein solubility responsive promoter is upregulated or downregulated when the target polypeptide is expressed in insoluble form, and host cells that express soluble target polypeptide

express the reporter gene at a decreased or increased level, respectively, compared to host cells that express insoluble target polypeptides. In identifying a promoter, the putative protein solubility responsive promoter is a heat shock promoter, a eukaryotic promoter or a prokaryotic promoter. Preferred **Array**: The target polypeptides in the **array** differ due to amino acid substitutions, deletions, or insertions compared to a reference amino acid sequence.

USE - The host cells are useful in monitoring the solubility of a target protein in a cell and in identifying mutations in the cell or in the polynucleotide encoding the target protein. The methods are useful in identifying variations in a protein biosynthetic process that alters the solubility of a target protein, in screening an expression library of recombinant clones that express soluble proteins, and in identifying an antibiotic agent.

EXAMPLE - No suitable example given. (69 pages)

L17 ANSWER 6 OF 10 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-04931 BIOTECHDS
TITLE: Immobilizing polypeptides, by contacting them to anchor molecules having nucleophile, so the ester/thioester groups of the polypeptides undergo trans-esterification to attach them to the anchor molecules on the surface; involving vector-mediated gene transfer for expression in host cell, for use in proteomics and high throughput screening
AUTHOR: NOCK S; SYDOR J
PATENT ASSIGNEE: ZYOMYX INC
PATENT INFO: WO 2001098458 27 Dec 2001
APPLICATION INFO: WO 2000-US19531 19 Jun 2000
PRIORITY INFO: US 2000-212620 19 Jun 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-114573 [15]
AN 2002-04931 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Immobilizing a polypeptide (I) comprising an ester or thioester (E/T) to a surface, by contacting (I) to an anchor molecule (II) comprising a nucleophilic group (N1) at 2 or 3 position relative to a second nucleophilic group, so the E/T undergoes a trans-esterification reaction with N1 to form an intermediate compound in which (I) is attached to (II) through N1, and attaching (II) to the surface.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an **array** (A1) of immobilized polypeptides attached to a surface (A1 comprises at least a first polypeptide species and a second polypeptide species and each of the polypeptide species are attached to a separate region of the surface in same orientation, and are folded in a secondary structure as required for a biological activity); (2) an **array** (A2) of immobilized polypeptides attached to a surface which comprises a number of surface regions (each surface region has attached to a polypeptide species and a polynucleotide that encodes the **polypeptide** species); (3) **screening** (M1) a library of nucleic acids to identify a nucleic acids that encodes a polypeptide having a desired activity, by expressing a number of fusion proteins, each of which is encoded by an expression cassette that comprises a member of the library of nucleic acids, an intein coding region, and an open reading frame that encodes a polypeptide that is displayed on a surface of a replicable genetic package (the fusion

proteins are displayed on the surface of a replicable genetic package) and screening the replicable genetic packages to identify those that display a polypeptide having the desired activity; (4) a nucleic acid (III) that comprises an expression cassette, comprising an insertion site at which a polynucleotide can be introduced into the expression cassette, an intein coding region (the carboxy terminus of the intein coding region is mutated so that it does not function as a splice junction for intein-mediated cleavage), and an open reading frame that encodes a polypeptide that is displayed on a surface of a replicable genetic package (the introduction of a polynucleotide at the insertion site results in an open reading frame that encodes a fusion protein which comprises a polypeptide encoded by the polynucleotide) which polypeptide is attached at its carboxyl terminus to an amino terminus of the intein, and the surface-displayed polypeptide is attached to the carboxy terminus of the intein; and (5) a kit for use in immobilizing one or more polypeptides containing E/T to a surface of a substrate, comprising an anchor molecule reagent for adapting E/T containing polypeptide to the surface.

WIDER DISCLOSURE - The following are also disclosed: (1) expression cassettes and expression vectors that facilitates the use of display on replicable genetic packages for initial screening, followed by intein-mediated derivatization of the polypeptide; (2) synthesizing arrays comprising (I); (3) biosensors, micromachined devices, and diagnostic devices that comprise the polypeptide arrays; and (4) transferring a target molecule to a reaction chamber, provides solution or condition that dissociates the target molecule from the affinity molecule.

BIOTECHNOLOGY - Preferred Method: The intermediate compound undergoes an intramolecular rearrangement in which the second nucleophilic group (N2) on (II) displaces N1, therefore forming a more stable bond between (II) and (I). In M1, the polypeptide encoded by the library member is released from the fusion protein by contacting the phage with a nucleophilic compound, which becomes attached to the polypeptide. The nucleophilic compound comprises a compound having N1 and N2. The nucleophilic compound is a 2-aminonucleophile or a 3-aminonucleophile or an aminothiol or a 3-aminothiol, and comprises a thiol or a hydroxyl. Preferred Molecule: (I) comprises a thioester. (II) comprises a 2-aminonucleophile e.g. 2-aminothiol or 3-aminonucleophile. (II) comprises a structure (S1) or (S2), and is attached to the surface prior to or after contacting (I). (II) comprises a functional group that can be covalently linked to a molecule that is attached to the surface, where the function group is selected from ketone, diketone, olefin, epoxide, aldehyde, reactive ester, isocyanate, thioisocyanate, carboxylic acid chloride, disulfide, sulfonate ester, maleimide, isomaleimide, N-hydroxysuccinimide, nitrilotriacetic acid, activated hydroxyl, haloacetyl, activated carboxyl, hydrazide, epoxy, aziridine, sulfonylchloride, acyl hydrazine, trifluoromethyldiaziridine, pyridyldisulfide, N-acyl-imidazole, imidazolecarbamate, vinylsulfone, succinimidylcarbonate, arylazide, anhydride, diazoacetate, benzophenone, isothiocyanate, isocyanate, imidoester, aminooxy or fluorobenzene. (II) comprises a **tag** group that can be non-covalently bound to a molecule that is attached to the surface. The **tag** comprises a binding domain derived from glutathione-S-transferase (GST), streptavidin

or green-fluorescent protein (GFP). The **tag** comprises a peptide that comprises an amino-terminal Cys, Thr or Ser. (I) comprises a non-natural amino acid, and E/T is chemically introduced onto (I) by chemical synthesis of the polypeptide. (I) is obtained by expressing a chimeric gene that encodes a fusion protein and contacting the fusion protein with a nucleophilic compound which releases the polypeptide from the intein at the splice junction and forms (I). The fusion protein comprises the polypeptide and an intein, or its functional portion, which is joined to the polypeptide at a splice junction at the amino terminus of the intein, where the carboxyl terminus of the intein lacks a functional splice junction. The nucleophilic compound is the anchor molecule and comprises a peptide. The peptide comprises a serine, threonine or cysteine at its amino terminus, the oxygen and sulfur of which are the nucleophilic groups that undergo the transesterification reaction. The nucleophilic compound comprises a thiol as the nucleophile.

The intein is an Int-n of a split intein and (II) comprises an amino acid sequence that comprises an Int-c of a split intein, where the Int-n and Int-c undergo an intein splicing reaction, therefore attaching (II) to (I). Int-n is derived from a dnaE-n gene and the Int-c is derived from a dnaE-c gene. The dnaE-n gene and dnaE-c gene are from a cyanobacterium. species e.g. Synechocystis sp.. The fusion protein is expressed in vitro or in vivo by introducing the chimeric gene into a host cell and incubating the host cell under conditions conducive to expression of the fusion protein. The surface on which (I) is immobilized, comprises a biochip comprising a non-sample surface and a number of sample portions that are elevated with respect to the non-sample surface, and each sample portion has attached to a single polypeptide species. The biochip comprises one or more materials selected from silicon, plastic, gold and glass. Alternately, the surface comprises a microparticle, and (I) is placed in contact with the surface using a microvolume dispenser that comprises a body and at least one vertical channel defined within the body, the channel being defined by at least one passive valve, where an interior surface defining at least one vertical channel is hydrophobic. The dispenser comprises a number of vertical channels defined within the body and arranged as an **array**. Each of the peptide species in A1, are covalently attached to the surface-bound linker by a 2-aminonucleophile ester bond e.g. 2-aminothioester bond, which undergoes an intramolecular rearrangement to form an amide bond. The linker is a non-peptide linker and the C-terminus of each of the polypeptide is attached to the surface. The linker comprises the structure S1 or S2. The expression cassette of (III) further comprises a promoter. (III) is a member of a library of polynucleotides such as library of cDNA molecules, genomic DNA fragments or recombination products. (II) comprises a NH2-NH-R and an aminooxy group, where R represents (II), E/T reacts with the reactive group, therefore forming a compound comprising (I) attached to (II) through a reactive group. Preferred Kit: The kit further comprises a DNA vector for introducing E/T into the polypeptide, where the vector is adapted to receive a nucleic acid sequence encoding the polypeptide to form a E/T polypeptide expression vector for expressing the polypeptide as an E/T polypeptide. The kit further comprises a chemical agent for introducing E/T into (I), and instructions for instructing a user to carry out the immobilization method using the kit. The kit further comprises a substrate for attaching (II) immobilizing

(I), where (II) is supplied attached to the surface of the substrate for later attaching (I) by a user. (I) is supplied with a kit precoupled with (II).

USE - The methods are useful for immobilizing polypeptides and for forming arrays of polypeptides (claimed). The immobilized polypeptides are useful for proteomics and high-throughput **screening**.

ADVANTAGE - The immobilized **polypeptides** are generally in the same orientation, are of full length and biologically active, and can be readily screened for a desired activity.

EXAMPLE - None given.(61 pages)

L17 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 2002:36295 CAPLUS
DOCUMENT NUMBER: 137:1515
TITLE: Nucleic acids and their encoded polypeptides from human tissues
INVENTOR(S): Tang, Y. Tom; Liu, Chenghua; Drmanac, Radoje T.
PATENT ASSIGNEE(S): Hyseq, Inc., USA
SOURCE: PCT Int. Appl., 1400 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 78
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064835	A2	20010907	WO 2001-US4927	20010226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001038347	A5	20010912	AU 2001-38347	20010226

PRIORITY APPLN. INFO.: US 2000-515126 A 20000228
US 2000-577409 A 20000518

AB The present invention provides a collection or library of 13,901 nucleic acid contig sequences assembled from expressed sequence tag or cDNA libraries isolated mainly by sequencing by hybridization (SBH), std. PCR, Sanger sequencing techniques, and in some cases, sequences obtained from one or more public databases. The cDNA libraries are from human tissue sources and nearest neighbor sequence homologies are provided. The invention also relates to the proteins encoded by such polynucleotides, along with therapeutic, diagnostic and research utilities for these polynucleotides and proteins. [This abstr. record is the fourth of four records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L17 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:747992 CAPLUS
DOCUMENT NUMBER: 135:284100
TITLE: Novel human nucleic acids and polypeptides
INVENTOR(S): Tang, Y. Tom; Asundi, Vinod; Shou, Ping; Xue, Aidong;

Ren, Feiyang; Zhang, Jie; Wang, Jian-rue; Xu, Chongjun; Yang, Yonghong; Zaho, Qing A.; Chen, Rui-hong; Wang, Dunrui; Goodrich, Ryle W.; Liu, Chenghua; Dramanac, Radoje T.

PATENT ASSIGNEE(S): Hyseq, Inc., USA
SOURCE: PCT Int. Appl., 336 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 78
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001075093	A1	20011011	WO 2001-US10484	20010330
WO 2001075093	C1	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6436703	B1	20020820	US 2000-668680	20000922
US 2002061567	A1	20020523	US 2000-728711	20001130
EP 1268762	A1	20030102	EP 2001-922987	20010330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:

US 2000-540217	A	20000331
US 2000-649167	A	20000823
US 2000-668680	A	20000922
US 2000-695618	A	20001130
US 2000-728711	A	20001130
US 2001-808701	A	20010314
WO 2001-US10484	W	20010330

AB The present invention provides 43 novel nucleic acids, novel polypeptide sequences encoded by these nucleic acids and uses thereof. The nucleic acids were obtained from cDNA libraries prepd. from various human tissues and in some cases isolated from a genomic library derived from human chromosomes using std. PCR, sequencing-by-hybridization signature anal., and Sanger sequencing techniques. Contigs were assembled using an expressed sequence **tag** (EST) as a seed. Tissue expression profiles, domain signature regions, and nearest neighbor sequence homologies are provided. These polynucleotides and polypeptides may be used in therapeutic, diagnostic, and research methods.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L17 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:842885 CAPLUS
DOCUMENT NUMBER: 136:396993
TITLE: Nucleic acids and their encoded polypeptides from human nervous system
INVENTOR(S): Rosen, Craig A.; Barash, Steven C.; Ruben, Steven M.
PATENT ASSIGNEE(S): Human Genome Sciences, Inc., USA
SOURCE: PCT Int. Appl., 1701 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 90
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001059063	A2	20010816	WO 2001-US1334	20010117
WO 2001059063	A3	20020704		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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WO	2001-US1348	A2 20010117
WO	2001-US1360	A2 20010117

AB The present invention relates to novel nervous system-elated polynucleotides, the polypeptides encoded by these polynucleotides herein collectively referred to as "nervous system antigens", and antibodies that immunospecifically bind these polypeptides, and the use of such nervous system polynucleotides, antigens, and antibodies for detecting, treating, preventing and/or prognosing disorders of the nervous system system, including, but not limited to, the presence of nervous system cancer and nervous system metastases. More specifically, 3324 isolated nervous system cDNA mols. and 7200 genomic DNA mols. are provided encoding novel human nervous system polypeptides. Novel nervous system polypeptides and antibodies that bind to these polypeptides are provided. Also provided

are vectors, host cells, and recombinant and synthetic methods for producing human nervous system polynucleotides, polypeptides, and/or antibodies. The invention further relates to diagnostic and therapeutic methods useful for diagnosing, treating, preventing and/or prognosing disorders related to the nervous system, including nervous system cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of polynucleotides and polypeptides of the invention. The invention further relates to methods and/or compns. for inhibiting or promoting the prodn. and/or function of the polypeptides of the invention.

[This abstr. record is the third of three records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L17 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:265594 CAPLUS
DOCUMENT NUMBER: 134:291149
TITLE: Human polypeptides and their encoding nucleic acids for use in angiogenesis and vascularization
INVENTOR(S): Gerritsen, Mary E.; Goddard, Audrey; Grimaldi, J. Christopher; Mehraban, Fuad
PATENT ASSIGNEE(S): Genentech, Inc., USA; Curagen Corporation
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001025433	A2	20010412	WO 2000-US27512	20001005
WO 2001025433	A3	20011129		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1224282	A2	20020724	EP 2000-970592	20001005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003511028	T2	20030325	JP 2001-528585	20001005

PRIORITY APPLN. INFO.: US 1999-158587P P 19991007
US 1999-162611P P 19991028
WO 2000-US27512 W 20001005

AB The present invention is directed to 5 novel polypeptides crit. for angiogenesis and vascularization, and to human nucleic acid mols. encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the

present invention. Compns. and methods are disclosed for stimulating or inhibiting angiogenesis and/or neo- or cardio-vascularization in mammals, including humans. Pharmaceutical compns. are based on polypeptides or antagonists thereto that have been identified for one or more of these uses. Disorders that can be diagnosed, prevented, or treated by the compns. herein include trauma such as wounds, various cancers, and disorders of the vessels including atherosclerosis.

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=> c his
C IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d his

     (FILE 'HOME' ENTERED AT 17:40:02 ON 26 JUN 2003)

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 17:40:16 ON 26 JUN 2003
L1          2293 S CHRISTIANS F?/AU OR COLE K?/AU
L2           197 S OLIGO TAG# OR NUCLEIC ACID TAG# OR OLIGONUCLEOTIDE TAG#
L3             0 S L1 AND (SCREEN### (4A) POLPEPTIDE#)
L4             1 S L1 AND L2
L5             0 S (SCREEN### (4A) POLPEPTIDE#)
L6          1884 S (SCREEN### (4A) POLYPEPTIDE#)
L7             2 S L6 AND L2
L8        319682 S PROBE ARRAY OR ARRAY OR MICROARRAY OR GENECHIP OR GENFLEX
ARR
L9          2795 S ((PLURALITY OR MULTIPLE OR MIXTURE) (4A) POLYPEPTIDE#)
L10           56 S L9 AND L8
L11            0 S L10 AND L2
L12            6 S L10 AND TAG
L13           25 S L9 AND TAG
L14            6 S L13 AND L8
L15          228 S L8 AND L6
L16           14 S L15 AND TAG
L17           10 DUP REM L16 (4 DUPLICATES REMOVED)

=>  s l1 and l8
L18           49 L1 AND L8

=> s l18 and tag
L19            1 L18 AND TAG

=> d l19

L19  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
AN   2003:355701  CAPLUS
DN   138:365121
TI   Methods for screening polypeptides using oligonucleotide tags and
     immobilization on probe arrays
IN   Christians, Fred; Cole, Kyle B.
PA   USA
SO   U.S. Pat. Appl. Publ., 24 pp.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 1
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     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
     ---------------    ----  --------       ---------------  --------
PI   US 2003087232       A1   20030508       US 2002-683613   20020124
PRAI US 2001-264635P     P    20010125


=> d his

     (FILE 'HOME' ENTERED AT 17:40:02 ON 26 JUN 2003)

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 17:40:16 ON 26 JUN 2003
L1          2293 S CHRISTIANS F?/AU OR COLE K?/AU
L2           197 S OLIGO TAG# OR NUCLEIC ACID TAG# OR OLIGONUCLEOTIDE TAG#
L3             0 S L1 AND (SCREEN### (4A) POLPEPTIDE#)
L4             1 S L1 AND L2
L5             0 S (SCREEN### (4A) POLPEPTIDE#)
L6          1884 S (SCREEN### (4A) POLYPEPTIDE#)
L7             2 S L6 AND L2
L8        319682 S PROBE ARRAY OR ARRAY OR MICROARRAY OR GENECHIP OR GENFLEX
ARR
L9          2795 S ((PLURALITY OR MULTIPLE OR MIXTURE) (4A) POLYPEPTIDE#)
L10           56 S L9 AND L8
L11            0 S L10 AND L2
L12            6 S L10 AND TAG
L13           25 S L9 AND TAG
L14            6 S L13 AND L8
L15          228 S L8 AND L6
L16           14 S L15 AND TAG
L17           10 DUP REM L16 (4 DUPLICATES REMOVED)
L18           49 S L1 AND L8
L19            1 S L18 AND TAG

=> dup rem l18
PROCESSING COMPLETED FOR L18
L20           18 DUP REM L18 (31 DUPLICATES REMOVED)

=> d ibib abs l20 1-18

L20  ANSWER 1 OF 18  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2003:355701  CAPLUS
DOCUMENT NUMBER:          138:365121
TITLE:                    Methods for screening polypeptides using
                          oligonucleotide tags and immobilization on probe
                          arrays
INVENTOR(S):              Christians, Fred; Cole, Kyle B.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 24 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
     ---------------    ----  --------       ---------------  --------
     US 2003087232       A1   20030508       US 2002-683613   20020124
PRIORITY APPLN. INFO.:                    US 2001-264635P  P  20010125
AB   In one aspect of the invention, methods are provided for the creation and
     screening of polypeptides that eliminates bacterial cloning and
individual
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screening. In preferred embodiments, the method involves partnering each protein with a unique DNA oligonucleotide tag that directs the protein to a unique site on the **microarray** due to specific hybridization with a complementary tag-probe on the **array**.

L20 ANSWER 2 OF 18 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2003258105 MEDLINE
DOCUMENT NUMBER: 22588901 PubMed ID: 12702811
TITLE: The effect of a single, temperature-sensitive mutation on global gene expression in Escherichia coli.
AUTHOR: Li Yong; **Cole Kyle**; Altman Sidney
CORPORATE SOURCE: Department of Molecular, Cellular and Developmental Biology, Yale University, New Haven, Connecticut 06520, USA.
CONTRACT NUMBER: GM19422 (NIGMS)
SOURCE: RNA, (2003 May) 9 (5) 518-32.
Journal code: 9509184. ISSN: 1355-8382.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030605
Last Updated on STN: 20030621
Entered Medline: 20030620

AB High-density DNA microarrays have been used to explore the genomic profiling of gene expression of a defective Escherichia coli strain with a temperature-sensitive mutation in the protein component of RNase P. A novel gene cluster was discovered in which two of the genes are known substrates of RNase P. The expression pattern of essential genes and gene discovery from intergenic regions, for which other new transcripts are found, are also discussed.

L20 ANSWER 3 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:583206 BIOSIS
DOCUMENT NUMBER: PREV200200583206
TITLE: High-density **GeneChip** oligonucleotide probe arrays.
AUTHOR(S): McGall, Glenn H. (1); **Christians, Fred C.**
CORPORATE SOURCE: (1) Affymetrix, Inc., 3380 Central Expressway, Santa Clara, CA, 95051: glenn_mcgall@affymetrix.com, fred_christians@affymetrix.com USA
SOURCE: Hoheisel, Joerg [Editor]. Advances in Biochemical Engineering Biotechnology, (2002) Vol. 77, pp. 21-42. Advances in Biochemical Engineering Biotechnology. Chip technology. print.
Publisher: Springer-Verlag New York Inc. 175 Fifth Avenue, New York, NY, 10010-7858, USA.
ISSN: 0724-6145. ISBN: 3-540-43215-9 (cloth).
DOCUMENT TYPE: Book
LANGUAGE: English

L20 ANSWER 4 OF 18 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002468221 MEDLINE
DOCUMENT NUMBER: 22214844 PubMed ID: 12227735
TITLE: High-density **genechip** oligonucleotide probe arrays.

AUTHOR: McGall Glenn H; **Christians Fred C**
CORPORATE SOURCE: Affymetrix, Inc, Santa Clara, CA 95051, USA..
glenn_mcgall@affymetrix.com
SOURCE: ADVANCES IN BIOCHEMICAL ENGINEERING/BIOTECHNOLOGY, (2002) 77 21-42. Ref: 60
Journal code: 8307733. ISSN: 0724-6145.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020914
Last Updated on STN: 20021026
Entered Medline: 20021025

AB High-density DNA probe arrays provide a highly parallel approach to nucleic acid sequence analysis that is transforming gene-based biomedical research. Photolithographic DNA synthesis has enabled the large-scale production of **GeneChip** probe arrays containing hundreds of thousands of oligonucleotide sequences on a glass "**chip**" about 1.5 cm2 in size. The manufacturing process integrates solid-phase photochemical oligonucleotide synthesis with lithographic techniques similar to those used in the microelectronics industry. Due to their very high information content, **GeneChip** probe arrays are finding widespread use in the hybridization-based detection and analysis of mutations and polymorphisms ("genotyping"), and in a wide range of gene expression studies.

L20 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:338541 CAPLUS
DOCUMENT NUMBER: 134:348929
TITLE: Novel enrichment and labeling strategy for preparation of ribonucleic acids from Escherichia coli
INVENTOR(S): **Christians, Fred C.**; Do, Duc; Gingeras, Thomas; Gunderson, Kevin; Miyada, Charles G.; Rosenow, Carsten; Wu, Kai; Yang, Qing
PATENT ASSIGNEE(S): Affymetrix, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032672	A1	20010510	WO 2000-US29865	20001030

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-162739P P 19991030
US 2000-191345P P 20000322

AB The presently claimed invention provides methods, compns., and app. for studying nucleic acids. Specifically, the present invention provides a novel enrichment and labeling strategy for ribonucleic acids with a bait mol. The bait mol. is capable of complexing specifically to unwanted target sequences within the nucleic acid sample, but is incapable of complexing with sequences from the population of interest. The bait mol. is contacted with the target sequences forming bait:target complexes which are then specifically removed from the nucleic acid sample. The remaining enriched population of interest is then fragmented and a signal moiety is attached to the fragments. In one embodiment, the invention provides enriching for a population of interest in a complex population by diminishing the presence of a target sequence. The invention provides a method for labeling prokaryotic mRNA comprising: obtaining a population of RNA from a prokaryotic organism: enriching mRNA by exposing them to a plurality of DNA bait mols. which are complementary to at least a portion of the stable RNA in said population under such conditions as to allow for the formation of DNA:RNA hybrids; exposing the DNA:RNA hybrids to RNAse H and DNAse I to remove both RNA and DNA, thus producing an enriched population of mRNA. In a further embodiment, the invention can be used to reproducibly label and detect extremely small amts. of nucleic acids.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 18 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001276317 MEDLINE
DOCUMENT NUMBER: 21260048 PubMed ID: 11359902
TITLE: PTEN expression causes feedback upregulation of insulin receptor substrate 2.
AUTHOR: Simpson L; Li J; Liaw D; Hennessy I; Oliner J; **Christians F**; Parsons R
CORPORATE SOURCE: Institute of Cancer Genetics, College of Physicians and Surgeons, Columbia University, New York, New York 10032, USA.
CONTRACT NUMBER: CA82783 (NCI)
CCA75553 (NCI)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (2001 Jun) 21 (12) 3947-58.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20021219
Entered Medline: 20010628

AB PTEN is a tumor suppressor that antagonizes phosphatidylinositol-3 kinase (PI3K) by dephosphorylating the D3 position of phosphatidylinositol (3,4,5)-triphosphate (PtdIns-3,4,5-P3). Given the importance of PTEN in regulating PtdIns-3,4,5-P3 levels, we used Affymetrix **GeneChip** arrays to identify genes regulated by PTEN. PTEN expression rapidly reduced the activity of Akt, which was followed by a G(1) arrest and

eventually apoptosis. The gene encoding insulin receptor substrate 2 (IRS-2), a mediator of insulin signaling, was found to be the most induced gene at all time points. A PI3K-specific inhibitor, LY294002, also upregulated IRS-2, providing evidence that it was the suppression of the PI3K pathway that was responsible for the message upregulation. In addition, PTEN, LY294002, and rapamycin, an inhibitor of mammalian target of rapamycin, caused a reduction in the molecular weight of IRS-2 and an increase in the association of IRS-2 with PI3K. Apparently, PTEN inhibits a negative regulator of IRS-2 to upregulate the IRS-2-PI3K interaction. These studies suggest that PtdIns-3,4,5-P3 levels regulate the specific activity and amount of IRS-2 available for insulin signaling.

L20 ANSWER 7 OF 18 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001150171 MEDLINE
DOCUMENT NUMBER: 21100319 PubMed ID: 11159908
TITLE: E2Fs regulate the expression of genes involved in differentiation, development, proliferation, and apoptosis.
AUTHOR: Muller H; Bracken A P; Vernell R; Moroni M C; **Christians F**; Grassilli E; Prosperini E; Vigo E; Oliner J D; Helin K
CORPORATE SOURCE: Department of Experimental Oncology, European Institute of Oncology, 20141 Milan, Italy.
SOURCE: GENES AND DEVELOPMENT, (2001 Feb 1) 15 (3) 267-85. Journal code: 8711660. ISSN: 0890-9369.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010315

AB The retinoblastoma protein (pRB) and its two relatives, p107 and p130, regulate development and cell proliferation in part by inhibiting the activity of E2F-regulated promoters. We have used high-density oligonucleotide arrays to identify genes in which expression changed in response to activation of E2F1, E2F2, and E2F3. We show that the E2Fs control the expression of several genes that are involved in cell proliferation. We also show that the E2Fs regulate a number of genes involved in apoptosis, differentiation, and development. These results provide possible genetic explanations to the variety of phenotypes observed as a consequence of a deregulated pRB/E2F pathway.

L20 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:383745 CAPLUS
DOCUMENT NUMBER: 133:13384
TITLE: Expression monitoring of BRCA1 regulated genes for detecting BRCA1 gene mutation, neoplasia diagnosis, and anti-cancer drug screening
INVENTOR(S): Oliner, Jonathan; **Christians, Fred**; Truong, Vivi; Harber, Daniel; Bean, James; Miklos, David; Harkin, Denis Paul
PATENT ASSIGNEE(S): Affymetrix, Inc. (A California Corporation), USA
SOURCE: Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1006181	A2	20000607	EP 1999-123859	19991201
EP 1006181	A3	20021218		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6258536	B1	20010710	US 1998-203677	19981201
US 2001051339	A1	20011213	US 2001-808352	20010315

PRIORITY APPLN. INFO.: US 1998-203677 A 19981201

AB A computer assisted method of detecting BRCA1 gene mutation using in-cell functional assay, and method of diagnosing neoplasia, and of identifying potential anti-cancer drugs by anal. of the expression of the BRCA1 regulated genes, are disclosed. The diagnosis method involves nucleic acid probe hybridization to transcription indicator such as mRNA, cDNA, or cRNA, in which probes are immobilized in an **array** to a solid support. The method also comprises BRCA1 gene sequence detn. and genotyping. The breast cancer susceptibility gene BRCA1 encodes a protein implicated in the cellular response to DNA damage, with postulated roles in homologous recombination as well as transcriptional regulation. To identify downstream target genes, we established cell lines with tightly regulated inducible expression of BRCA1. High-d. oligonucleotide arrays were used to analyze gene expression profiles at various times following BRCA1 induction. Twenty three genes and ESTs were identified as having increased expression following BRCA1 induction. A major BRCA1 target was the DNA damage-responsive gene GADD45 and the early immediate gene Early Growth Response 1 (EGR1). Expression of a couple of genes, Ki-67 and prothymosin .alpha., was repressed. Induction of BRCA1 triggered apoptosis through activation of c-Jun N-terminal kinase/stress-activated protein kinase (JNK/SAPK), a signaling pathway potentially linked to GADD45 gene family members. The p53-independent induction of GADD45 by BRCA1 and its activation of JNK/SAPK suggest a pathway for BRCA1-induced apoptosis.

L20 ANSWER 9 OF 18 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001172716 MEDLINE
DOCUMENT NUMBER: 21119578 PubMed ID: 11272889
TITLE: Molecular profiling of clinical tissues specimens: feasibility and applications.
AUTHOR: Emmert-Buck M R; Strausberg R L; Krizman D B; Bonaldo M F; Bonner R F; Bostwick D G; Brown M R; Buetow K H; Chuaqui R F; **Cole K A**; Duray P H; Englert C R; Gillespie J W; Greenhut S; Grouse L; Hillier L W; Katz K S; Klausner R D; Kuznetzov V; Lash A E; Lennon G; Linehan W M; Liotta L A; Marra M A; Munson P J; Ornstein D K; Prabhu V V; Prang C; Schuler G D; Soares M B; Tolstoshev C M; Vocke C D; Waterston R H
CORPORATE SOURCE: Pathogenetics Unit, Laboratory of Pathology, National Cancer Institute, Bethesda, Maryland, USA.. mbuck@helix.nih.gov
SOURCE: JOURNAL OF MOLECULAR DIAGNOSTICS, (2000 May) 2 (2) 60-6. Ref: 52
Journal code: 100893612. ISSN: 1525-1578.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329

L20 ANSWER 10 OF 18 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1999457495 MEDLINE
DOCUMENT NUMBER: 99457495 PubMed ID: 10525416
TITLE: Acquisition of novel catalytic activity by the M1 RNA ribozyme: the cost of molecular adaptation.
AUTHOR: **Cole K B**; Dorit R L
CORPORATE SOURCE: Department of Ecology and Evolutionary Biology, Yale University, 165 Prospect St, New Haven, CT, 06511, USA.
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1999 Oct 1) 292 (4) 931-44.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991104

AB The ribonucleoprotein RNase P is a critical component of metabolism in all known organisms. In Escherichia coli, RNase P processes a vast **array** of substrates, including precursor-tRNAs and precursor 4. 5S RNA. In order to understand how such catalytic versatility is achieved and how novel catalytic activity can be acquired, we evolve the M1 RNA ribozyme (the catalytic component of E. coli RNase P) in vitro for cleavage of a DNA substrate. In so doing, we probe the consequences of enhancing catalytic activity on a novel substrate and investigate the cost this versatile enzyme pays for molecular adaptation. A total of 25 generations of in vitro evolution yield a population showing more than a 1000-fold increase in DNA substrate cleavage efficiency (kcat/KM) relative to wild-type M1 RNA. This enhancement is accompanied by a significant reduction in the ability of evolved ribozymes to process the ptRNA class of substrates but also a contrasting increase in activity on the p4.5S RNA class of substrates. This change in the catalytic versatility of the evolved ribozymes suggests that the acquired activity comes at the cost of substrate versatility, and indicates that E. coli RNase P catalytic flexibility is maintained in vivo by selection for the processing of multiple substrates. M1 RNA derivatives enhance cleavage of the DNA substrate by accelerating the catalytic step (kcat) of DNA cleavage, although overall processing efficiency is offset by reduced substrate binding. The enhanced ability to cleave a DNA substrate cannot be readily traced to any of the predominant mutations found in the evolved population, and must instead be due to multiple sequence changes dispersed throughout the molecule. This conclusion underscores the difficulty of correlating observed mutations with changes in catalytic behavior, even in

simple biological catalysts for which three-dimensional models are available.

L20 ANSWER 11 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:184910 BIOSIS
DOCUMENT NUMBER: PREV199900184910
TITLE: Gene expression profiles occurring during prostate cancer progression.
AUTHOR(S): **Cole, K. A. (1)**; Gillespie, J. W.; Herring, J.; Duray, P. H.; Englert, C. R.; Ornstein, D. K.; Petricoin, E. F.; Pan, S.; Pfeiffer, J.; Johnson, C.; Munson, P. J.; Linehan, W. M.; Liotta, L. A.; Emmert-Buck, M. R.
CORPORATE SOURCE: (1) Natl. Cancer Inst., Bethesda, MD 20892 USA
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (March, 1999) Vol. 40, pp. 408-409. Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania,
USA April 10-14, 1999 American Association for Cancer Research
. ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L20 ANSWER 12 OF 18 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1999112705 MEDLINE
DOCUMENT NUMBER: 99112705 PubMed ID: 9915499
TITLE: The genetics of cancer--a 3D model.
AUTHOR: **Cole K A**; Krizman D B; Emmert-Buck M R
CORPORATE SOURCE: Pathogenetics Unit, Laboratory of Pathology, National Cancer Institute, Bethesda, Maryland 20892, USA.
SOURCE: NATURE GENETICS, (1999 Jan) 21 (1 Suppl) 38-41. Ref: 47
Journal code: 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990209
Last Updated on STN: 19990209
Entered Medline: 19990127

AB Gene expression microarrays hold great promise for studies of human disease states. There are significant technical issues specific to utilizing clinical tissue samples which have yet to be rigorously addressed and completely overcome. Precise, quantitative measurement of gene expression profiles from specific cell populations is at hand, offering the scientific community the first comprehensive view of the in vivo molecular anatomy of normal cells and their diseased counterparts. Here, we propose a model for integrating-in three dimensions-expression data obtained using the **microarray**.

L20 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:529685 CAPLUS
TITLE: Metalloporphyrins as a platform for the development of
new antimalarial lead compounds.
AUTHOR(S): Wright, David W.; Ziegler, Jim; **Cole, Kelly A.**

; Evans, Kathy
CORPORATE SOURCE: Department Chemistry and Biochemistry, Duquesne University, Pittsburgh, PA, 15282-1530, USA
SOURCE: Book of Abstracts, 216th ACS National Meeting, Boston,
August 23-27 (1998), MEDI-200. American Chemical Society: Washington, D. C.
CODEN: 66KYA2
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB We report that metal substituted porphyrin's act as inhibitors to hemozoin
formation, a crit. detoxification biopolymer of malarial parasites, and may, therefore, have potential applications as anti-malarial agents. The polymer extension is prevented by the formation of hemin:metalloporphyrin complexes through pi-stacking interactions, the same mode postulated for the quinoline drugs. We have extended these studies by increasing the "plane of aromaticity" using related macrocycles such as phthalocyanine. Addnl., these compds. have been used as inhibitors to heme binding at the nucleation site within histidine-rich protein models. The diverse **array** of available porphyrin ligands and large no. of suitable metals makes the metalloporphyrin system an excellent platform on which to
base structure-activity relationships in ongoing studies for the development of new antimalarial agents which target all aspects of hemozoin formation.

L20 ANSWER 14 OF 18 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 1999063897 MEDLINE
DOCUMENT NUMBER: 99063897 PubMed ID: 9845739
TITLE: Histopathology and molecular biology of ovarian epithelial tumors.
AUTHOR: Chuaqui R F; **Cole K A**; Emmert-Buck M R; Merino M J
CORPORATE SOURCE: Laboratory of Pathology, National Cancer Institute, Bethesda, MD, USA.
SOURCE: ANNALS OF DIAGNOSTIC PATHOLOGY, (1998 Jun) 2 (3) 195-207.
Ref: 92
Journal code: 9800503. ISSN: 1092-9134.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19990106
AB Carcinogenesis in the ovary presents special features related to that organ. First, the preinvasive or even invasive lesions are difficult to detect, which explains why most cases are diagnosed at an advanced stage. Second, the group of tumors of low malignant potential (borderline tumors)
are still a controversial category of ovarian lesions. Finally, familial ovarian tumors represent an interesting hereditary model of carcinogenesis
at the molecular level. Flow cytometry and immunohistochemistry for proliferative markers or oncogenes provide important prognostic information in patients with ovarian tumors. Molecular data, such as loss

of heterozygosity at specific genetic loci, also have been correlated with prognosis. Clonality studies in patients with multiple ovarian/pelvian lesions analyzing chromosome X inactivation patterns and genetic deletions or mutations have contributed to the understanding of the origin of these lesions. New technologies to study gene expression patterns, such as cDNA library construction and DNA **microarray** technologies, are being applied to study histologic phases of tumor progression, such as normal, preinvasive, and tumor tissues. It is hoped that these studies will contribute important information not only for a better understanding of the process of carcinogenesis, but also for assessing the biology and behavior of individual tumors, determining patient prognosis, and eventually influencing therapy.

L20 ANSWER 15 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 9

ACCESSION NUMBER: 1978:44941 BIOSIS
DOCUMENT NUMBER: BR14:44941
TITLE: ANALOG SOLUTION FOR ELECTRICAL CAPACITY OF MEMBRANE COVERED CUBES IN CUBIC **ARRAY** AT HIGH CONCENTRATION.
AUTHOR(S): **COLE K S**
SOURCE: Biophys. J., (1977) 17 (2), 22A.
CODEN: BIOJAU. ISSN: 0006-3495.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: Unavailable

L20 ANSWER 16 OF 18 MEDLINE DUPLICATE 10

ACCESSION NUMBER: 77058057 MEDLINE
DOCUMENT NUMBER: 77058057 PubMed ID: 1069286
TITLE: Analogue solution for electrical capacity of membrane-covered cubes in cubic **array** at high concentration.
AUTHOR: **Cole K S**
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1976 Nov) 73 (11) 4003-6.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197701
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19980206
Entered Medline: 19770129

AB Earlier measurements have shown that the equations derived for the resistance of suspension of spheres apply up to a volume concentration of 100% for close-packing forms. They have also shown, by a resistance-capacitance analogue, that they apply for the capacity of a close-packing of membrane-covered square cylinders in square **array**, approximating muscle and nerve. The present work is an extension of the two-dimensional to a three-dimensional **array** of membrane-covered cubes in a cubic **array**. It is found by measurements of a three-dimensional electrolytic analogue that the capacitance is indeed expressed by an extension of the analytic solution at low concentrations

up to 100% volume concentration of the membrane-covered form, such as epithelial tissues. There is thus at least one example each of two-and three-dimensional forms which conform to the low concentration analysis up to 100% volume and so give a basis for the extensions to other and more complicated forms to complete a survey to work begun by Fricke in 1923.

L20 ANSWER 17 OF 18 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 76:57179 SCISEARCH
THE GENUINE ARTICLE: BE662
TITLE: ANALOG SOLUTION FOR ELECTRICAL CAPACITY OF MEMBRANE COVERED SQUARE CYLINDERS IN SQUARE **ARRAY** AT HIGH-CONCENTRATION
AUTHOR: **COLE K S (Reprint)**
CORPORATE SOURCE: NINCDS, IRP, LAB BIOPHYS, BETHESDA, MD, 20014
COUNTRY OF AUTHOR: USA
SOURCE: BIOPHYSICAL JOURNAL, (1976) Vol. 16, No. 2, pp. A173.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L20 ANSWER 18 OF 18 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 76102673 MEDLINE
DOCUMENT NUMBER: 76102673 PubMed ID: 1061082
TITLE: Analogue solution for electrical capacity of membrane covered square cylinders in square **array** at high concentration.
AUTHOR: **Cole K S**
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1975 Dec) 72 (12) 4936-9. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197603
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19760330

AB Analytical solutions of Laplace equations have given the electrical characteristics of membranes and interiors of spherical, ellipsoidal, and cylindrical cells in suspensions and tissues from impedance measurements, but the underlying assumptions may be invalid above 50% volume concentrations. However, resistance measurements on several nonconducting, close-packing forms in two and three dimensions closely predicted volume concentrations up to 100% by equations derived from Maxwell and Rayleigh. Calculations of membrane capacities of cells in suspensions and tissues from extensions of theory, as developed by Fricke and by Cole, have been useful but of unknown validity at high concentrations. A resistor analogue has been used to solve the finite difference approximation to the Laplace equation for the resistance and capacity of a square **array** of square cylindrical cells with surface capacity. An 11 x 11 **array** of resistors, simulating a quarter of the unit structure, was separated into intra- and extra-cellular regions by rows of capacitors corresponding to surface membrane areas from 3 x 3 to 11 x 11 or 7.5% to 100%. The extended Rayleigh equation predicted the cell concentrations and membrane capacities to within a few percent from boundary resistance and capacity measurements at low frequencies. This single example suggests that analytical solutions for other, similar two- and three-dimensional

problems may be approximated up to near 100% concentrations and that there
may be analytical justifications for such analogue solutions of Laplace equations.

=> d his

(FILE 'HOME' ENTERED AT 17:40:02 ON 26 JUN 2003)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 17:40:16 ON 26 JUN 2003

```
L1          2293 S CHRISTIANS F?/AU OR COLE K?/AU
L2           197 S OLIGO TAG# OR NUCLEIC ACID TAG# OR OLIGONUCLEOTIDE TAG#
L3             0 S L1 AND (SCREEN### (4A) POLPEPTIDE#)
L4             1 S L1 AND L2
L5             0 S (SCREEN### (4A) POLPEPTIDE#)
L6          1884 S (SCREEN### (4A) POLYPEPTIDE#)
L7             2 S L6 AND L2
L8        319682 S PROBE ARRAY OR ARRAY OR MICROARRAY OR GENECHIP OR GENFLEX
ARR
L9          2795 S ((PLURALITY OR MULTIPLE OR MIXTURE) (4A) POLYPEPTIDE#)
L10           56 S L9 AND L8
L11            0 S L10 AND L2
L12            6 S L10 AND TAG
L13           25 S L9 AND TAG
L14            6 S L13 AND L8
L15          228 S L8 AND L6
L16           14 S L15 AND TAG
L17           10 DUP REM L16 (4 DUPLICATES REMOVED)
L18           49 S L1 AND L8
L19            1 S L18 AND TAG
L20           18 DUP REM L18 (31 DUPLICATES REMOVED)
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=> s l2 and mRNA
L21           54 L2 AND MRNA

=> s l21 and l8
L22           13 L21 AND L8

=> s l22 and translat?
L23            2 L22 AND TRANSLAT?

=> d ibib abs l23 1-2

L23   ANSWER 1 OF 2  BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2003-13218  BIOTECHDS
TITLE:            Producing self-assembled protein microarray, by
                  using in vitro translation system to produce
                  properly folded proteins and locating proteins in known
                  regions on microarray by adding self-addressing
                  oligonucleotide tags;
                     luciferase, FLAG fusion protein microarray
                     construction
AUTHOR:           OLEINIKOV A V
PATENT ASSIGNEE:  COMBIMATRIX CORP
PATENT INFO:      WO 20030018773 6 Mar 2003
APPLICATION INFO: WO 2002-US28223 27 Aug 2002
PRIORITY INFO:    US 2001-315253 27 Aug 2001; US 2001-315253 27 Aug 2001
DOCUMENT TYPE:    Patent
```

LANGUAGE: English
OTHER SOURCE: WPI: 2003-312888 [30]
AN 2003-13218 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Producing (M) self-assembled protein **microarray** with several proteins in discrete locations, involves preparing cDNA's each encoding a different protein, transcribing cDNA and **translating** **mRNA** in a cell-free **translation** system to synthesize synthetic proteins, attaching oligonucleotide (ONT) tag sequence and localizing the proteins on an ONT **microarray** device.

DETAILED DESCRIPTION - Producing (M) self-assembled protein **microarray** with several proteins in discrete locations comprises: (a) preparing several cDNAs, each encoding a different protein, where each cDNA comprises a promoter region and a coding region and segregating each cDNA into separate chambers; (b) transcribing each cDNA into a **mRNA**, where the **mRNA** will form a protein encoded by the coding region of the cDNA; (c) **translating** each **mRNA** in a cell-free **translation** system to synthesize several synthetic proteins each including a first binding moiety incorporated in it, where each **mRNA** molecule can be used to **translate** several synthetic proteins to increase yield, (d) attaching a second binding moeiety that specifically binds to the first binding moiety, where the second binding moiety further comprises an ONT tag sequence to form ONT-addressed synthetic protein, and localizing the ONT-addressed synthetic proteins onto an ONT tag **microarray** device, where the ONT tag **microarray** device comprises several ONT sequences at known locations, where then ONT sequences are designed to be complementary to an ONT tag sequence on the second binding moiety, where each ONT-addressed protein localizes to its predefined complementary region on the ONT tag **microarray** device through nucleic acid hybridization. Alternatively, the method involves amplifying each cDNA with specific primers to produce several synthetic proteins each containing a peptide tag at either terminus, incorporating in each synthetic protein a first binding moiety by in vitro **translation**, capturing each synthetic protein on a solid phase using an antibody directed against the peptide tag, adding a second binding moiety to each synthetic protein in each container, where the second binding moiety is multivalent and binds specifically to the first binding moiety, adding ONTs labeled with the first binding moiety to bind to the second binding moiety, forming an ONT-tagged protein complex, where the different tag ONTs are designed in a way that they do not cross-hybridize to each other, eluting each ONT-tagged protein complex from the solid phase, and mixing the protein complexes from separate containers and incubating the mixture with an ONT tag **microarray** device, where each ONT-tagged protein complex localizes to its predefined complementary region on the ONT tag **microarray** device, forming a self-assembled protein **microarray** having several proteins in discrete locations. An INDEPENDENT CLAIM is also included for a protein **microarray** having several proteins in discrete locations, produced by (M).

BIOTECHNOLOGY - Preferred Method: The cDNA's are prepared through PCR techniques and further comprise a tag region that codes on expression for a protein tag, where the protein tag sequence is used to affinity bind the synthetic protein in order to wash out unbound first binding moiety. The **translation** further comprises adding cell or liver microsomes in order to provide for eukaryotic cell glycosylation of the synthetic protein at N-linked or O-linked glycosylation sites. The first binding moiety is biotin or its derivative, and the second binding moiety

is streptavidin or its derivative, or the first binding moiety is an antigen, and the second binding moiety is an antibody or its fragment that binds to the antigen. The first binding moiety is a biotin moiety that is linked to the synthetic peptide through Lys residues. The ONT tag sequence attached to the second binding moiety is 12-100 nucleotides in length, where at least 12 nucleotides are exactly complementary to their corresponding tag **array** ONT sequence on the **microarray** device. The method further involves incorporating in each **translated** protein in a first binding moiety, removing the free first binding moiety by binding the synthetic protein through an affinity third binding moiety that binds to the peptide tag sequence and is attached to a solid phase, and washing to remove free or unbound first binding moiety.

USE - (M) is useful for producing self-assembled protein **microarray** having several proteins in discrete locations.

ADVANTAGE - The method is capable of automation to provide **microarray** devices with theoretically unlimited number of different and separately functional proteins for binding, enzymatic activity or other biochemical interactions with a properly folded protein. The yield of protein is significantly greater, as the **mRNA** molecule generated are used repeatedly to make many copies of a protein. When synthetic protein is bound to a solid support through a peptide tag, streptavidin tetramers can bind this protein through incorporated biotin moieties only through one biotin-binding site leaving three other sites available for interaction with biotin. The three remaining sites can be filled in using specific ONTs coupled with biotin moieties providing specific tagging for the complex of synthetic protein with incorporated biotins bound to SA. Thus, this step eliminates the need for chemical coupling of SA with specific oligonucleotides and makes the method available for automated techniques.

EXAMPLE - Luciferase control DNA was used to prepare DNA coding for luciferase-FLAG fusion protein by conventional methods of PCR with appropriate sequences. A commercially available FLAG epitope was added for immobilizing the **translated** fusion protein. The final construct included T7 RNA-polymerase promoter, Kozak sequence for initiation of **translation**, luciferase coding sequence fused to FLAG-coding sequence, and stop-codon. This DNA was transcribed and **mRNA** was purified. This **mRNA** was used for **translation** in vitro. Anti-FLAG M2 resin was used to capture each synthetic protein in separate tube after **translation**. 25 mul of resin was added and incubated with **translation** mixtures overnight at 4degreesC. Resin was washed 5 times in TBS buffer (10 mM Tris-HCl, pH 7.6, 150 mM NaCl). Enhanced green fluorescent protein (EGFP) bound to the resin was visible (as green fluorescence) after this step under appropriate blue light. The synthetic proteins were tagged with specific oligonucleotides. 100 mul of 0.1 mg/ml streptavidin (SA) in 10% bovine serum albumin (BSA) in phosphate buffered saline (PBS) solution was added to each tube and incubated for several hours at 4degreesC to bind to biotinylated synthetic proteins captured on the anti-FLAG resin. The resin was washed 3 times with TBS and excess of biotinylated oligonucleotides (ONTs) was added to each tube to bind to tag the synthetic protein-SA complexes. Each synthetic protein was tagged with a specific ONT. Tagged complexes were mixed together with NaCl. This mixture was incubated with a **microarray** device containing ten different capturing ONTs made by in situ electrochemistry. Two of which

were complementary to the two biotinylated ONTs used to tag synthetic proteins. Microarrays were or were not preincubated with blocking solution to reduce non-specific binding. Incubation of tagged protein complexes was performed at 37-40degreesC for 1-16 hours. Microarrays were washed 3 times in 2xTBS solution to remove non-bound complexes. After this washing step, protein microarrays were considered prepared and ready for analysis of the bound proteins in different biochemical assays. (40 pages)

L23 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:355701 CAPLUS
DOCUMENT NUMBER: 138:365121
TITLE: Methods for screening polypeptides using **oligonucleotide tags** and immobilization on probe arrays
INVENTOR(S): Christians, Fred; Cole, Kyle B.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 24 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003087232	A1	20030508	US 2002-683613	20020124

PRIORITY APPLN. INFO.: US 2001-264635P P 20010125

AB In one aspect of the invention, methods are provided for the creation and screening of polypeptides that eliminates bacterial cloning and individual screening. In preferred embodiments, the method involves partnering each protein with a unique DNA **oligonucleotide tag** that directs the protein to a unique site on the **microarray** due to specific hybridization with a complementary tag-probe on the **array** .

=> d his

(FILE 'HOME' ENTERED AT 17:40:02 ON 26 JUN 2003)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS' ENTERED AT 17:40:16 ON 26 JUN 2003

L1 2293 S CHRISTIANS F?/AU OR COLE K?/AU
L2 197 S OLIGO TAG# OR NUCLEIC ACID TAG# OR OLIGONUCLEOTIDE TAG#
L3 0 S L1 AND (SCREEN### (4A) POLPEPTIDE#)
L4 1 S L1 AND L2
L5 0 S (SCREEN### (4A) POLPEPTIDE#)
L6 1884 S (SCREEN### (4A) POLYPEPTIDE#)
L7 2 S L6 AND L2
L8 319682 S PROBE ARRAY OR ARRAY OR MICROARRAY OR GENECHIP OR GENFLEX ARR
L9 2795 S ((PLURALITY OR MULTIPLE OR MIXTURE) (4A) POLYPEPTIDE#)
L10 56 S L9 AND L8
L11 0 S L10 AND L2
L12 6 S L10 AND TAG
L13 25 S L9 AND TAG

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L14            6 S L13 AND L8
L15          228 S L8 AND L6
L16           14 S L15 AND TAG
L17           10 DUP REM L16 (4 DUPLICATES REMOVED)
L18           49 S L1 AND L8
L19            1 S L18 AND TAG
L20           18 DUP REM L18 (31 DUPLICATES REMOVED)
L21           54 S L2 AND MRNA
L22           13 S L21 AND L8
L23            2 S L22 AND TRANSLAT?

=> s mRNA and translated product
L24          282 MRNA AND TRANSLATED PRODUCT

=> s mRNA and polypeptide#
L25        43809 MRNA AND POLYPEPTIDE#

=> s l25 and (l2 or tag)
L26          594 L25 AND (L2 OR TAG)

=> s l26 and l8
L27           74 L26 AND L8

=> l27 and probe
L27 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l27 and probe
L28           24 L27 AND PROBE

=> d ibib abs l28 1-28

L28   ANSWER 1 OF 24  BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2003-14319  BIOTECHDS
TITLE:            Printed material useful as a delivery and storage system for
                  oligomer and/or polymer, comprises a support having an
                  oligomer and/or polymer applied on it;
                     printed material, and DNA amplification for use in
                     diagnosis
AUTHOR:           HAYASHIZAKI Y
PATENT ASSIGNEE:  DNAFORM KK; RIKEN KK
PATENT INFO:      WO 20030027991 3 Apr 2003
APPLICATION INFO: WO 2002-JP9766 24 Sep 2002
PRIORITY INFO:    JP 2001-291249 25 Sep 2001; JP 2001-291249 25 Sep 2001
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2003-354676 [33]
AN    2003-14319  BIOTECHDS
AB    DERWENT ABSTRACT:
      NOVELTY - A printed material (1) (I) comprising at least one support
      having at least one oligomer and/or polymer applied on it, is new.
           DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1)
      preparing (I) involves applying the oligomer and/or polymer on the
      support before or after printing; (2) delivering (M1) and/or storing at
      least one oligomer and/or polymer applied on at least one support for a
      printed material, comprising applying the oligomer and/or polymer on the
      support before or after printing and delivering or storing the printed
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material; (3) synthesis (M2) of cDNA, comprising: (a) applying at least a set of primers for the amplification and/or ligation of exons of a support and/or printed material; (b) recovering the at least set of primers from the support and/or printed material; (c) mixing the set of primers with template DNA, enzyme and buffer; and (d) carrying out the amplification and/or ligation; (4) a kit comprising a support and/or printed material comprising at least one primer or a set of primers applied on it; and (5) a kit for the synthesis of cDNA and/or full-length cDNA from genomic template, comprising at least one support and/or printed material comprising at least one set of primers, for the amplification and/or ligation of exons, applied on it.

BIOTECHNOLOGY - Preferred Material: The printed material is in unbound form, or in bound form where the support is not bound in the material or the support is bound as a page of the bound material. Optionally, (I) comprises at least two supports which are not bound together. The printed material is composed of at least one printed page. The printed material is chosen from journals, magazines, articles, books, booklets, leaflets, pamphlets, reports, posters, cards and labels. The support is a water-insoluble, water-dissolvable and/or water-soluble support. The water-insoluble support comprises cellulose as a major component. The water-soluble support is in the form of wafer. Preferably, the support is in the form of card(s). The oligomer is chosen from oligonucleotide, oligopeptide, oligosaccharide, peptide nucleic acid (PNA) or its mixture. The polymer is chosen from polynucleotide, **polypeptide**, polysaccharide, PNA or its mixture. The oligomer or polymer is a fragment or a complete molecule. The oligonucleotide or polynucleotide is selected from genomic DNA, cDNA, RNA, **mRNA**, PNA or its combination. Preferably, the oligonucleotide or polynucleotide is chosen from a fragment, an expressed sequence **tag** (EST) sequence, long strand, full-coding and full-length sequence. The oligonucleotide or polynucleotide comprises one or more amplification and/or ligation primer and/or oligonucleotide **probe**(s). (I) comprises a set of primers for the amplification and ligation of exons of a gene comprised in genomic DNA. The set of primers comprises a pair of primers for each exon of the desired gene, at least one primer of each pair of one exon being also partially complementary to the next exon. The set of primers are suitable for synthesizing cDNA and/or full-length cDNA from genomic DNA by amplification and ligation of the exons of a gene. (I) further comprises one or more enzymes and/or buffer. Preferred Method: The oligomer and/or polymer is applied on the support by fixing or printing it on the support. In (M1), the oligomer and/or polymer is applied on the support by applying or adhering a solution of the oligomer and/or polymer directly to the support by a pin, syringe or ink-jet printer. (M1) further involves recovering the oligomer and/or polymer by elution from the support. The recovery is carried out by inserting the support in a device and performing the elution and recovery from the support automatically by the device. The support is preferably in the form of card which comprises a bar- code, a **chip** or a label containing information about the position of the oligomer and/or polymer on the card. The operator selects the oligomer and/or polymer of interest

and the device automatically elutes and recovers the oligomer and/or polymer of interest from the support. In (M2), after the application step, the support and/or printed material is stored and/or delivered. The enzyme and buffer are applied on the support and/or printed material during application step. Preferred Kit: The support and/or material further comprises at least one of enzyme, buffer, genomic DNA, cDNA, RNA, **mRNA**, PNA, plasmid, vector and nucleic acid. The kit for synthesis of cDNA further comprises at least one enzyme for the amplification and/or ligation step, and/or buffer.

USE - (M2) is useful for synthesizing DNA, where the product of amplification and/or ligation is cDNA and/or full- length cDNA which is recovered and used for determination of nucleotide insertion/deletion, single nucleotide polymorphism (SNP) and sequencing analysis, in a diagnostic method for determination of nucleotide insertion/deletion, or SNP analysis. Optionally, the cDNA and/or full-length cDNA is useful for the peptide, **polypeptide** or protein expression. (All claimed.) The printed material is useful in research applications, or for providing scientists with oligomer and/or polymers from the printed materials easily and immediately.

ADVANTAGE - From the printed material, at least an oligomer and/or polymer can be obtained immediately and directly, without need to make a request for it. The oligomers and/or polymers can be delivered and stored easily with reduced labor and time while eliminating the need to use special equipment or facilities. Thus, the printed material is a quick, efficient and inexpensive sample delivery system.

EXAMPLE - Three RIKEN plasmid cDNA clones with various cDNA insert sizes (744, 2440 and 5460 base pairs) were inserted into pBluescript. Plasmid DNA comprising the cDNA clones were purified. The plasmid DNA was dissolved in TE (10 mM Tris-HCl (pH 8.0), 1 mM EDTA). DNA concentration was adjusted to 0.1 micro-g/micro-l. At this step an inert dye, was added to the solution in order to facilitate identification of spot position on the support at the time of recovery. 0.1 micro-l of the plasmid DNA solution prepared as above was transferred onto 60 MDP paper used as DNA sheet using a 96-pin tool. Spotted positions were easily identified by being spotted in a marked position on the paper. After drying the paper in air for more than 30 minutes, DNA was extracted from the sheet as follows. The piece of 60 MDP paper (0.4x0.4 mm) containing the selected DNA spot was cut out from the sheet and placed into a PCR tube followed by addition of 50 micro-l of PCR solution. PCR solution contained the following PCR primers: 21M13 5'-TGTAAAACGACGGCCAGT-3' and 1233-Rv 5'-AGCGGATAACAATTTCACACAGGA-3', 0.2 mM each of dATP, dGTP, dCTP and dTTP and in presence of various concentrations of MgCl. After centrifuging the resulting solution, the PCR cycle was initiated. Aliquots of PCR solutions were analyzed using 1 % agarose gel electrophoresis. Results showed that the cDNA inserts were amplified successfully, preferably at Mg2+ concentration of 5.3 mM. This test confirmed that the chosen conditions allowed for an efficient spotting and extraction of DNA.(91 pages)

L28 ANSWER 2 OF 24 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2003-13578 BIOTECHDS
TITLE: New nucleic acid for human maternal antigen that embryos

require protein, useful e.g. in diagnosis and treatment of female infertility;
baculo virus vector-mediated gene transfer and expression in host cell for recombinant protein production for use in
disease diagnosis and gene therapy

AUTHOR: WEISS B; LESSL M; PETERS-KOTTIG M; BECKMANN G
PATENT ASSIGNEE: SCHERING AG
PATENT INFO: EP 1285964 26 Feb 2003
APPLICATION INFO: EP 2002-90246 12 Jul 2002
PRIORITY INFO: DE 2001-1039874 10 Aug 2001; DE 2001-1039874 10 Aug 2001
DOCUMENT TYPE: Patent
LANGUAGE: German
OTHER SOURCE: WPI: 2003-302814 [30]
AN 2003-13578 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - New nucleic acid (I) comprises: (i) a fully defined 3926 (S1) or 3830 (S3) nucleotide sequence as given in the specification; (ii) an equivalent of (i) within the degeneracy of the genetic code; or (iii) a sequence that hybridizes to (i) or (ii) under stringent conditions, encoding a protein with the function of the human MATER (maternal antigen that embryos require) protein.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) any nucleic acid (Ia) that encodes proteins comprising fully defined sequences of 1162 (S2) and 1143 (S4) amino acids as given in the specification; (2) a **polypeptide** (II) encoded by (I) or (Ia); (3) antibodies (Ab) against (II); (4) antisense molecules against (I); (5) vector containing at least one copy of (I) or (Ia); (6) cells transformed with (I), (Ia) or the vector of (5); (7) test system for identifying effectors (X) of (II); (8) diagnostic method for determining autoantibodies against MATER in body samples or the amount of MATER (protein or **mRNA**) in eggs; (9) a DNA **chip** that carries at least one oligonucleotide corresponding to the (partial) sequence, or complement, of sequences (S1) or (S3); and (10) inhibiting activity of (II) in cells by contact with (X).

BIOTECHNOLOGY - Preferred Nucleic Acid: (S1) and (S3) are human sequences. (3) is a splice variant that lacks exon 4. The coding region extends from positions 1-3489 and 1-3432, respectively. **mRNA** transcribed from the MATER gene is found predominantly in ovary, testis and placenta. Preparation: The coding regions of both splice variants are amplified with the primers 5'-TAGTTGGCATTCTTTTGATG 5'-ATGGAAGGAGACAAATCGCTC and then cloned into baculoviruses or eukaryotic expression vectors, particularly for expression as a fusion with a His **tag**.

ACTIVITY - Antiinfertility; Contraceptive; Antiinflammatory; Immunosuppressive; Gynecological. No details of tests for these activities are given.

MECHANISM OF ACTION - Modulation of MATER, at protein or **mRNA** levels. MATER is an NTP(nucleoside triphosphate)ase associated with apoptosis; a defect in MATER activity causes growth arrest at the 2-cell stage of fertilized eggs.

USE - (I) is used for recombinant expression of the corresponding **polypeptide** (II) and probes based on (I) are used to determine the corresponding **mRNA**. (II) are used to prepare antibodies (Ab), useful for detection and quantification of (II) in usual immunoassays, also as contraceptives. Any of (I), (II), or cells transfected with (I) can be used to identify effectors (X) of (II), while

(I), (II), Ab and antisense sequences against (I) are targets for preparing agents useful for treating disorders associated with the MATER (maternal antigen that embryos require) gene and/or protein. Particularly (X) are used to treat infertility associated with endometriosis (claimed), and also ovarian dysfunction, autoimmune premature ovarian failure, inflammation, autoimmune diseases and female infertility, and as contraceptives. Measurements of autoantibodies against MATER in body samples or MATER protein or **mRNA** in eggs is useful for diagnosis of female infertility, particularly by detecting mutations in the MATER gene with a DNA **chip**. (31 pages)

L28 ANSWER 3 OF 24 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2003-10464 BIOTECHDS
TITLE: Novel isolated human glycosyltransferase, designated 47174 **polypeptides**, useful for treating central nervous system disorder, pain or pain related disorder, neurodegenerative disorders or renal disorder; vector-mediated gene transfer, expression in host cell and transgenic animal for recombinant protein production, drug screening and gene therapy
AUTHOR: KAPELLER-LIBERMANN R
PATENT ASSIGNEE: KAPELLER-LIBERMANN R
PATENT INFO: US 2002164746 7 Nov 2002
APPLICATION INFO: US 2001-973457 9 Oct 2001
PRIORITY INFO: US 2001-973457 9 Oct 2001; US 2000-238849 6 Oct 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-238309 [23]
AN 2003-10464 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - An isolated human glycosyltransferase **polypeptide** (I), designated 47174 comprising a sequence of 603 amino acids (aa) fully defined in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated nucleic acid molecule (NAM) (II) comprising a sequence (S1) of 2572 or 1812 nucleotides fully defined in the specification, or a NAM which encodes (I); (2) a host cell (III) containing (II); (3) an antibody (Ab) or its antigen binding fragment that selectively binds to (I); (4) producing (I); (5) a kit (IV) comprising a compound that selectively binds to (I) or (II), and instructions for use; (6) detecting (M1) presence of (II) in a sample, by contacting the sample with a nucleic acid **probe** or primer which selectively hybridizes to the NAM and determining whether the nucleic acid **probe** or primer binds to the NAM in the sample; (7) inhibiting (M2) aberrant activity of 47174-expressing cell, by contacting 47174 expressing cell with a compound that modulates the activity or expression of (I), in an amount which is effective to reduce or inhibit the aberrant activity of the cell; and (8) treating or preventing (M3) a disorder characterized by aberrant activity of 47174-expressing cell, in a subject, by administering to a subject a compound that modulate the activity or expression of (II) such that the aberrant activity of 47174-expressing cell is reduced or inhibited.

WIDER DISCLOSURE - The following are also disclosed as new: (1) an

2002:575354 CAPLUS

DOCUMENT NUMBER: 137:104764
TITLE: Nucleic-acid programmable protein arrays
INVENTOR(S): Labaer, Joshua; Lau, Albert Y.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059601	A1	20020801	WO 2002-US1882	20020122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002192673	A1	20021219	US 2002-55432	20020122

PRIORITY APPLN. INFO.: US 2001-263607P P 20010123

AB Arrays of polypeptides are generated by translation of nucleic acid sequences encoding the **polypeptides** at a **plurality** of addresses on the **array**.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

of gene expression from the data. However, the reproducibility study from Incyte showed that the level of detectable differential expression was calculated to be approximately+/-1.74. Consequently, any elements with observed ratios at least1.8 between cancer and normal were deemed differentially expressed. DiaDexus **microarray** candidates sequences were sequences for lung cancer and the lung specific genes (LSGs) had a sequence of 1449, 3825, 2315, 300, 4347, 2116, 4474, 777, 3195, 949, 14917, 1823, 869, 799, 1731, 662, 336, 3300, 349, 4665, 437 or 355 base pairs fully defined in the specification. Absolute values at least1.8 were considered to be above background levels, and were, therefore significant. The relative levels of expression showed that the expression of the 1449 base pair **mRNA** was higher than background in 7 of cancer tissue samples selected (the 1449, 3825, 2315, 300, 4347, and 2116 base pair sequence samples). The 3825 base pair **mRNA** expression was higher than background in 3 of the cancer tissue samples, the 2315 base pair **mRNA** expression was higher than background in 3 of the cancer tissue samples, the 300 base pair **mRNA** expression was higher than background in 3 of the cancer tissue samples, the 4347 base pair **mRNA** expression was higher than background in 5 of the cancer tissue samples, and the 2116 base pair **mRNA** expression was higher than background in 4 of the cancer tissue samples. An additional 16 clones were also identified by the same type of experiments. These additional clones all showed from 30-80% overexpression in cancer tissue samples. (197 pages)

L28 ANSWER 18 OF 24 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-11665 BIOTECHDS
TITLE: Novel 25204 **polypeptide** which is a human short chain dehydrogenase/reductase **polypeptide**, useful for treating sarcoidosis, jaundice, multiple sclerosis, restrictive cardiomyopathy, hypertension, Burkitt lymphoma; human enzyme gene transfer, antisene, ribozyme, DNA primer, DNA **probe** and drug screening, useful for gene therapy and diagnosis
AUTHOR: MEYERS R; WILLIAMSON M
PATENT ASSIGNEE: MILLENNIUM PHARM INC
PATENT INFO: WO 2001057195 9 Aug 2001
APPLICATION INFO: WO 2000-US3335 1 Feb 2000
PRIORITY INFO: US 2000-496010 1 Feb 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-256042 [30]
AN 2002-11665 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - An isolated human short chain dehydrogenase/reductase 25204 **polypeptide** is new.
DETAILED DESCRIPTION - (I) is a human short chain dehydrogenase/reductase 25204 (SDR) and is: (a) encoded by a nucleic acid (NA) having a nucleotide sequence that is 60% identical to NA having a fully defined sequence of 1097 (S1) nucleotides as given in specification; (b) a naturally occurring allelic variant of a **polypeptide** having a fully defined sequence of 292 amino acids (S2) as given in the specification, where the **polypeptide** is encoded by a NA molecule which hybridizes to the complement of (S1) or a fully defined sequence of 879 nucleotides (S3) as given in specification,

under stringent conditions; or (c) a **polypeptide** having a sequence of (S2) or its fragment having 15 contiguous amino acids of (S2). INDEPENDENT CLAIMS are also included for the following: (1) an